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on the

I.A.M.S. / I.C.M.R. SEMINAR

on

'HEALTH OF WOMEN'

HELD ON 23RD DECEMBER, 1975

at

MAULANA AZAD MEDICAL COLLEGE

NEW DELHI

Ann Indian Acad Med Sci, 12, 4, Oct-Dec 1976

Special Number on 'Health of Women' Seminar

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Ann Indian Acad Med Sci, 12, 4, Oct—Dec, 1976

Editorial

New Horizons in Health Care

A characteristic of modern social change is planned development. Planning is facile, when something new is to be attempted, but becomes complex when it is presaddled with centuries of inertia and sloth. The task of planning the basic health needs of vast numbers of people is stupendous, and the sheer magnitude of the problem is enough to daunt anyone but the intrepid. In many countries less than 15 per cent of rural population and other unprivileged groups have access to health services. In the less developed countries the most needy constitute about 80 per cent of the population. The other factors with which one has to contend are abject poverty, illiteracy and ignorance about basic health terets, and above all a hostile environment to concepts of change. The redeeming feature in the dismal picture is a wind of change which is now blowing all over the world waking up the masses from age-old slumber and invoking in them a desire to improve their own lot.

The specific task of health retrieval and reconstruction in all its manifold dimensions of curative, preventive and promotive health is a part of the total dynamic economic programme visualised by the national leadership. The task is to be commonly shared by both Government and voluntary efforts. The learned societies like the Indian Academy of Medical Sciences can study the precepts and philosophies and assist in working out a tangible plan of action which is feasible, economical and can be translated into practice in a relatively brief span of time. The magnitude of the task predetermines the official role in implementation. Even at that stage independent evaluation, feed back and suggestion of corrective methods based on periodic appraisals may be well taken up by national societies.

The lessons of pioneer efforts in this country and in other parts of the globe all highlight the factors of acceptance of health programmes as those which are component of total developmental plans with its emphasis on adequate food, housing, clothing, accessibility and safe water supply, which are community based and community supported, which give universal coverage but emphasises the need of more vulnerable sections of the community with special reference to maternal, child care, nutrition and family planning, and which dovetails into the existing social patterns without raising unnecessary conflicts. The created institutions must at the same time fit in with the community as well as with the health delivery system of the country.

The Director General of the WHO in his report to the 28th World Health Assembly has succintly summarised the dimensions of Primary Health Care as follows:-

"The primary health care is taken to mean a health approach which integrates at community level all the elements necessary to make an impact on the health status of the people. Such an attempt has to be a part of national health care system. It is an expression or response to the fundamental human needs of how can a person know of, and be assisted in the actions required to live a healthy life and where can a person go if he/she needs relief from pain or suffering. A response to such needs must be a series of simple and effective measures in terms of cost, technique and organisation, which are easily accessible to the people in need and which assist in improving the living conditions of individuals, families and communities. These include preventive, promotive, curative, rehabilitative health measures and community development activities".

The concept of a community based health worker, who has more than one function in total developmental plan, and who is the now retrieved missing link between the community and grass root health worker is gradually gaining ground. The type of the community health worker and his modus of operation being dependent on local cultural patterns, will of necessity be different in different parts of the world.

The Savar project of Bangladesh started in 1972 aims at giving comprehensive health care with a small hospital as referral base with 11 sub-centres delivered by locally trained village health workers drawn from the student community, trained locally in immunisation, health education, family planning advice and curative treatment for minor ailments. A novel aspect of the programme is a scheme of self insurance for almost all types of health services in return of modest monthly premiums.

The barefoot doctor of China has attracted enough attention now to merit only a mention in passing.

A community development approach in Central Jawá to raise health standards has drawn the conclusions that community life continues without external intervention but to raise living standards, concrete activities of an organized and planned nature are essential. The broad concept of development should be based on network of of activities both physical and mental to create the proper climate for overall improvement of quality of life taking into consideration the inter-relationship of man and his environment. In this context the community health programme should include both curative and preventive services, but place emphasis on activities that increases the potential of man for healthy life.

Sudan has an extremely well developed system of training and utilisation of traditional nurse midwifes—many of whom are illiterate, relying heavily on skill to identify problems at appropriate time and undertake appropriate measures, and also to identify problems which require referral.

The Jamkhed project at Maharashtra has also underlined the imperative need of building rapport with the community leadership and identifying priority areas of community's felt needs. The budget of the health programme is in accordance with the needs of the community. Curative care accounting for 30 per cent, community health programmes 60 per cent and administration the rest. The community volunteers trained locally were easily fitted with the medical programmes in the community. The master minds behind the project give an unequivocal affirmative to the question, can such a project be replicated ?

Against the background of a wealth of information on the subject, indigenous as well as global that the community level health workers scheme has been formulated. The scheme was approved by the April 1976 meeting of the Central Council of Health and Family Planning and aims at bringing elementary health care, curative, preventive and promotive at door steps to give a total coverage of the population.

It is estimated that our total population is over 600 million which is about 15 per cent of the total world population, living in 2.4 per cent of world's land area. Approximately 80 per cent of our population live in 600 thousand villages in accessible as well as difficult terrains.

The problems of the rural areas have been foremost in the minds of planners since the days of Health Survey and Development Committee (Bhore Committee, 1946). The Committee's recommendations from the basis of rural health service based on Primary Health Centre manned by a health team headed by medical personnel and sub-centres manned by auxillaries.

Due to historical reasons various national health programmes developed vertically, and only a few years back steps were initiated to integrate four important programmes of family planning, small pox eradication, malaria control and trachoma control into one multipurpose health workers scheme. The implementation of the programme has been tardy due to resurgence of malaria, extended activities of family planning programme, as well as the herculean effort required to make the country smallpox free. This is all the more reason to give effect to the community health workers' scheme. If the scheme works well, and it will, if it gets community support, the obstacles of implementation of the complimentary multipurpose workers scheme will have been reduced.

The scheme, as formulated, aims at recruiting primary and middle school teachers employed by Government or boards under Governmental control, village post masters, **gram sevak** and **sevikas** and trained indigenous midwives. Initially the scheme is likely to be put into action in districts chosen for implementation of multipurpose health workers' scheme, and may involve as many as 75,000 workers. The personnel after a short term intensive training in the various aspects of health care, curative, preventive and promotive, will function in their own areas to provide advice and health care to the populace. The worker will also have close liaison with the health set up.

The acceptability of the worker by the community is presumed, as usually teachers and postmasters have good credibility in rural Indian society. The indigenous midwife has been an instrument of health delivery from ages immemorial.

Probably the emphasis on selection of teachers and postmasters is to keep proper tabs to prevent escalation of the programme into quackery. The danger does exist, and thus the precaution might be sagacious, but in the light of experience gained, the harnessing of the newly aroused youth power in the country may not be ignored in future expansions of the programme.

A recent joint UNICEF/WHO study has come out with the opinion "Health care delivery systems—public and private, national and international, curative and preventive, peripheral, intermediate and central—must be considered as a whole.

In the health services, over centralization of authority and executive responsibility may prevent effective and adequate delivery at the periphery. It tends to lead to an over concentration of personnel, institutions and facilities, and so to the maldistribution of resources. Central authorities become too far removed from the bulk of the people and loose touch with the community needs and expectations. Present systems of reporting seldom convey to the centre the full picture of requirements". Alternative approaches to meeting basic health needs in developing may not agree to the total opinion specially in view of awakened communities the world over and the vigilant media, the caution may be needed and inbuilt precaution taken at a formative stage to avoid the predictable pitfalls.

—R. K. SANYAL

Scientific Session I

Demographic Aspects

Ann Indian Acad Med Sci, 12, 4, Oct.—Dec., 1976

The Increasing Sex Ratio in India

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The increasing masculinity ratio of Indian population during the past several decades is a curious phenomenon from socio-demographic-economic angles. The sex ratio† (males per 100 females) had increased from 102.9 in 1901 to 105.3 in 1931 to 107.5 in 1971 as can be seen in Table I.

Table I. Sex ratio (males per 100 females), 1901-71.

Period	Sex Ratio
1901	102.9
1911	103.8
1921	104.7
1931	105.3
1941	105.8
1951	105.7
1961	106.3
1971	107.5

Source : Sample Registration System : **Sex Composition in India**, SRS Analytical Series, No. 4, 1972, Vital Statistics Division, Office of the Registrar General, India, New Delhi, Table 1, p. 3.

The increasing sex ratio in the present century has emanated from the differential rate of growth of the population of the two sexes in favour of the males in all the census decades excepting 1941-51 which was affected by partition resulting in refugee influx most probably dominated by the females. The trend in rates of growth of the two can be seen in Table II.

Mainly three hypotheses have been put forward from time to time to explain the anomalous situation characterized by an increasing excess of males over females in India. The first hypothesis purporting to explain the masculinity of Indian population, has been that the censuses underenumerate women to a greater extent than men. The factors responsible for the greater omission of females than of males include the

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*Lecturer in Economics.

†The sex ratio can be defined also as the number of females per 100 males. In Indian census sex ratio is defined as the number of females per 1000 males.

'low estimation in which females are held', 'the reticence of the people on all matters connected with their female relatives' and the failure of enumerators to comprehend that the counting of females was important (Visaria, 1968). (These reasons had been given in some earlier census reports of the country). However, such a hypothesis is untenable due to the following reasons: (a) It can be reasonably assumed that each successive census in this country has been marked by improvement in quality and in completeness in coverage and thus the increasing imbalance in the sex ratio in every successive decade cannot be attributed merely to the omission of females; (b) The sample verification following the 1951 and the 1961 Censuses which were meant to check the coverage of the counts indicated the persistence of only a slight tendency to greater under-enumeration of females than that of males; (c) In the recent years, Sample Registration System which is a 'dual reporting system' based on continuous enumeration by a local enumerator and by the supervisor every six months on a retrospective basis, also indicates a sex ratio favourable to males confirming the census results. For example, the SRS data related to the rural areas of many States in India indicated the sex ratio to be 106.1 in 1969 (Sample Registration System, 1972).

Table II. Inter-census growth rate by sex 1901—1971.

	Decennial Growth Rates	
Period	Male	Female
1901-11	6.3	5.4
1911-21	0.1	0.8
1921-31	11.2	10.6
1931-41	14.5	13.9
1941-51	13.3	13.5
1951-61	22.0	21.3
1961-71	22.5	24.0

Source : Same as in Table I, (p.5).

The second hypothesis asserts that the sex ratio in India is higher than the usual ones existent in the western countries due to the higher sex ratio at birth (number of males per 100 females among live births) in the former than in the latter. On the basis of the data for 1912-14 in India, S.de Jastrzebski, an Assistant Registrar General of Great Britain, inferred that the differences in the sex ratios at birth in the different parts of the country were attributable to the variations in the race in the different areas. Similarly, race was thought to be an important factor in determining the degree of masculinity at birth in the different countries of the world (Visaria, 1968). Besides race, the caste system prevalent in India was considered to be the main factor causing high sex ratio : "caste therefore would appear to be of definite assistance to the Hindu in his superlative anxiety for male children; moreover, since the higher the caste the stricter, in the past at any rate, the ban on external exogamy, this tendency would show more patently in the higher caste and explain why the proportion of females to males increases in inverse ratio to social status" (Natrajan, 1972). Further, it has been held that the widely-prevalent preference for male children in India, Pakistan and Ceylon and the associated festivity characterizing a male birth cause the reporting of the same to be more complete than that of the female birth The rebuttal or acceptance of the above mentioned factors purporting to explain the higher sex ratio at birth in India than in the other countries of the world is conditioned by a priori establishment of the fact of higher sex ratio at birth in India empirically. The available data, for various countries of the world however, do not support such a contention. As can be seen in Table III, the sex ratio at birth during the 60s varied between 108.8—102.5 in the different countries, of the world and thus the sex ratio at birth in India (107.8) cannot be considered very high.

Table III clearly indicates that the sex ratio at birth is favourable to males in India as in all the countries listed in the table. This implies that the demographic profile of this country from the point of view of sex ratio is not biologically widely divergent from the pattern generally observed in the world but that certain socio-economic factors reflected in the differential mortality conditions of the two sexes in India, hinder the change in the sex ratio in favour of the females. In the Census of India, 1901 it was stated that the possible causes of higher female mortality in India were (a) female infanticide,* (b) a comparatively greater neglect of females, especially at the earlier ages, (c) premature cohabitation and child bearing coupled with unskillful midwifery, (d) hard work in the case of lower classes, and (e) general adverse conditions of climate, nutrition, house accommodation and the like (Natrajan, 1972). The 1911 Census, while acknowledging the difficulty of ascertaining the extent of murder of female infants, contended that the neglect of female infants in India was of two kinds : there was the deliberate neglect with the object of causing death, which was practically infanticide in a more cruel form, and there was the half conscious neglect, due partly to habit and partly to the parents' great solitude for their sons. The boys were better clad, and when ill, were more carefully tended. They were allowed to eat their fill before anything was given to the girls. In poor families, when there was not enough for all, it was invariably the girls who suffered.

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*Female infanticide was supposed to be on the wane at this time but was suspected to be widely prevalent in Sindh Rajputana and United Provinces throughout the 19th century due to the prevalence of extremely high sex ratio in these regions in the beginning of the 20th century.

Table III. Sex ratio at birth and death in selected countries.

Country	Period	Sex ratio at birth	Sex ratio at death
A. *Africa*			
South Rhodesia (106.1)*	(1963-67)	107.4	137.5
Zambia (104.0)	(1963-67)	106.6	112.0
Mauritius (100.7)	(1963-67)	103.1	110.7
B. *North America*			
Canada (100.7)	(1963-67)	105.5	140.6
Costa Rica (100 2)	(1963-67)	104.8	115.5
Gautemala (100.1)	(1963-67)	105.6	106.4
Mirmuda (97.9)	(1963, '67, 68)	108.8	122.7
Puerto Rico (98.8)	(1963-67)	105.6	127.2
United States (96.4)	(1963-67)	105.0	129.9
C. *South America*			
Argentina (100.0)	(1963-66)	104.0	144.3
Guyana (99.3)	(1963-67)	102.5	117.0
Chile (97.2)	(1963-67)	103.7	122.8
D. *Asia*			
Ceylon (108.2)	(1963-67)	103.4	123.8
Singapore (107.1)	(1963-68)	105.1	149.4
India (Rural (106.1)	(1969)	107.8	96.2
Israel (102.0)	(1963-67)	106.5	123.3
Japan (96.5)	(1963-67)	105.9	118.1
E. *Europe*			
Albania (105.6)	(1963-67)	106.0	101.3
Bulgaria (96.2)	(1963-68)	105.8	115.1
Sweden (99.8)	(1963-67)	106.1	117.1
Norway (99.3)	(1963-68)	106.4	119.1
Italy (95.9)	(1963-66)	105.5	113.1
Switzerland (95.3)	(1963-68)	105.4	109.7
France (95.1)	(1963-67)	104.9	107.0
Greece (95.0)	(1963-68)	106.7	103.9
United Kingdom (94.7)	(1963-68)	105.8	107.4
Spain (94.1)	(1963-67)	105.6	107.4
Hungary (93.7)	(1963-68)	106.8	107.3
Eastern Germany (95.1)	(1963-68)	106.1	91.6
West Berlin (75.4)	(1963-67)	105.4	78.9

Source : Same as in Table I, pp. 23-24 (Table 25).

*Figures within brackets are sex ratio of the population as a whole.

In this way, even when there was no deliberate intention of hastening a girl's death, she was at a great disadvantage as compared with her brothers in the struggle for life (Natrajan, 1972). The situation is not very different today as can be seen from Table IV depicting the infant mortality rate by sex.

Table IV : Infant mortality and its components by sex, rural, 1969*.

Sex	Age of Infants			
	<7 days	7-28 days	29 days to 6 months	7 to 12 months
Male	44.4	29.4	38.1	20.4
Female	41.0	34.9	47.7	24.5

Source : Sample Registration System : **Infant Mortality in India,** SRS Analytical Series No. 1, 1971, Vital Statistics Division, Office of the Registrar General, New Delhi, Table 4, p. 6.

*Excludes Bihar, Himachal Pradesh, Madhya Pradesh, Nagaland, Orissa, West Bengal and Union Territories.

It can be observed that the risk of dying is more in the case of male infants than female infants during the period of one week after birth in India as is generally expected. But such an advantage of the female infants over their male counterparts gets reversed after 7 days and more distinctly after 28 days of the child's birth. The perceptible disparity in the post-natal mortality rates (deaths occurring to 1000 babies who are in the age group one-month to 12 months) of the two sexes in favour of the males, clearly reflects the differential nutritional and other associated medical care given to male and female children in this country. The greater risks to female lives remain unabated even after one year of birth till the age of 4 and then gradually the differences between the sexes get narrower till the middle of teen ages and again widens till the age of 34 years. Thereafter, the age-specific death rates of females remain somewhat lower than the same of the males as can be seen in Table V.

The Model Registration Unit of the Vital Statistics Division in this country in its report, **Causes of Death 1971—A Survey,** indicated almost the same trend : the sex ratio (here it is defined as the number of females per 1000 males) at death declined from 1086.4 in the age-group 1-4 years to 976.1 in the age-group 5-14 years, increased to 1[illegible]0[illegible].2 in the age-group 15—34 years declining again to the range of 700 in the age-group 35+in 1971 (Model Registration Unit Report, 1971). In contrast, in the advanced countries, deaths amongst the males are higher than female deaths in all the age-groups. In the reproductive span of life (15-49) also, male deaths predominate the female deaths as can be seen in Table VI.

Table V : Age specific death rate, SRS, rural, 1968 and 1969.

Age-group	Death Rate			
	1968		1969	
	Male	Female	Male	Female
0—4	59.12	66.82	58.32	70.16
5—9	5.53	6.26	5.79	7.71
10—14	2.26	2.60	2.99	2.72
15—19	1.99	3.34	2.09	4.22
20—24	2.65	5.09	3.88	5.54
25—29	3.19	6.92	3.73	5.50
30—34	3.76	5.98	4.07	6.35
35—39	6.23	6.09	6.54	6.05
40—44	7.67	7.92	8.52	7.60
45—49	12.68	9.18	13.17	9.36
50—59	18.99	15.35	22.36	17.76
60+over	65.08	60.54	71.21	66.48
All ages	17.46	18.96	18.23	20.11
15—49	4.77	6.01	5.32	6 05

Source : Same as in Table I, p. 13, (Table 8).

Table V 'A'. Sex ratio of deaths by age at death, SRS, rural 1968 and 1969.

Year	Age-group					
	0—4 (1)	5—14 (2)	15—24 (3)	25—34 (4)	35—44 (5)	45—54 (6)
1968	94.8	95.9	56.8	53.7	108.3	146.7
1969	88.3	92.7	61.4	64.8	120.1	140.9
		55+ (7)	15—49 (8)		All ages (9)	
1968		114.6	83.3		98.5	
1969		116.0	91.7		96.2	

Source : Same as in Table V, p. 13 (Table 9).

Table VI. Sex Ratio of deaths by age at death (till 49 years) for selected countries.

Country	Sex ratio by age at death 0—4	5—14	15—49
U. S. A. (1966)	137.7	157.4	179.2
Ceylon (1963)	107.9	101.1	100.3
Japan (1965)	134.1	165.7	149.1
Singapore (1966)	122.0	133.3	177.2
U. K. (1966)	136.3	166.9	160.2
India (1969) Rural	88.3	92.7	91.7

Source : Same as in Table 1, p. 27 (Table 28).

The differential mortality rates of the two sexes in favour of the males in the age-group 15-45 years are caused by the prevalence of extremely high maternal mortality rates in India. Maternal mortality rate (per 100,000 live births) was 32 in U.S.A. in 1965, 25 in U. K. in 1970, 72 in Taiwan in 1966 and 573 in 1968 (Visaria, 1968) and 376.3 in India (rural) in 1971 (Model Registration Unit Report, 1971). The high maternal mortality rate in this country is the result of the operation of the following factors.

In the reproductive phase of woman's life in India, marriage is her only destiny conferred upon her by the society traditionally, it is almost her only means of support and the sole justification of her existence. Consequently celibacy is almost non-existent as is revealed by the 1971 census returns that in the age-group 15+, only 11 per cent of the women of the nation were unmarried.

However, in the familistic society of India, marriage is not an end in itself but is only a means to procreation, to achieve motherhood, as only on becoming a mother that the woman becomes a partner in the family rights and her marital life can perpetuate with relative ease and tranquility at familial and societal levels. However, the achievement of the the desired size of family is severely constrained by the prevalence of the high rate of infant mortality. About one-third of all deaths in India in 1961 were infant deaths. That there occurred no marked departure from this trend during the last decade is clearly evident from Table VII which also indicates the extremely low infant mortality rate in the other countries of the world.

Table VII. Infant mortality rate in selected countries.

Country	Infant mortality (per 1000 live births)	Crude death rate (per 1000 population)
Japan (1968)	15	6.8
U. K. (1968)	19	11.9
U. S. A. (1968)	21	9.7
U. S. S. R. (1968)	26	7.7
Ceylon (1967)	48	7.5
Mexico (1968)	64	9.6
Burma (1967)	67	N. A.
U. A. R. (1967)	116	15.8
India (1961 - Census)*	146	22.0
India (1968 - SRS) Rural	137	16.8
India (1969 - SRS) Rural	140	19.1

Source : Same as in Table IV, p. 17 (Table 11).

*The figure pertaining to infant mortality rate for 1961 has been taken from : Census Centenary 1972, India. **Pocket Book of Population Statistics**, Table Vs 3, p. 97, Registrar General and Census Commissioner, New Delhi, 1972.

The prevalence of high infant mortality rate leads to frequent pregencies as under the highly uncertain conditions of the child's survival, the desired size of family (the desired size of family is quite large in India due to the marked preference for sons amongst the people and due to the great utility of a child following its contribution to family labour and to it being source of old age security) can be achieved by having a large number of births. This tendency is further strengthened by the fact that the first born child is at greatest risk of survival. In India, one out of every five first-born children dies in the first year and one of every four infant deaths is a first-born child (Gulick, 1971). The death of the very first child leads to a drastic decline in the probability of the survival of the subsequent children in the minds of the parents and therefore birth orders frequently reach five or six in many families apart from the prevalence of widespread illiteracy in the population resulting in lack of awareness and practice of methods of family limitation being the factor largely responsible for such high birth orders. The SRS' findings have revealed that as late as in 1971-72, 22. 57 per cent of the total births in the rural areas belonged to the birth orders of six and above as can be seen in Table VIII.

Table VIII. Per cent distribution of live births by birth order, 1961 (whole country), 1969 and 1971-1972 (rural).

Birth orders	Per cent live birth in		
	1961[1]	1969[2] (rural)	1971-72[3] (rural)
First	20.1	20.5	19.5
Second	17.6	18.1	17.2
Third	15.5	16.4	15.5
Fourth	13.1	14.5	13.9
Fifth	10.9	11.6	11.3
Sixth and above	22.8	18.9	22.6

Source : 1. Gulick, 1971.

2. Sample Registration System : SRS, Vol. IX, No. 3, July 1975, Table 8, p. 19, Registrar General, India, Ministry of Home Affairs, New Delhi.

Frequent pregnancies affect maternal health in a marked manner. In a study of socio-cultural factors in the epidemiology of hypertension among the Zulu of South Africa it has been revealed that amongst the Zulu women of urban location near Durban, the incidence of hypertension increased with the number of children. Jaffe and Polgar analysed nearly 350,000 births in the United States and illustrated the inter-relationship of age and parity as determinants of maternal deaths. They found that the maternal mortality rate increased steadily with advancing age from 5.1 per 100,000 live births for mothers under 20 years of age to 34.3 for women of 40 years of age and over. Within each age group the maternal mortality rate increased with parity, except for the age-group 40 years and over, where women not having any child had a higher mortality rate than women who had four or more previous births (Chatterjee, 1972). Maternal death is often stated to be caused by haemorrhage or shock and anaemia which are most common in women having a large number of pregnancies. The effects of multiparity and maternal health in Jordan were studied by Aksheh (1972) who found that a large number of pregnancies increased the risk of rupture of uterus, postpartum haemorrhage, pre-eclamptic toxaemia, accidental haemorrhage, placenta praevia disproportion and anaemia. Model Registration Unit of the Vital Statistics Division (1971), Ministry of Home Affairs in India reported that approximately 19 per cent of all maternal deaths per 100,000 live births in the rural areas in 1971, were caused by anaemia of pregnancy and 13.5 per cent of the same were caused by post-partum haemarrhage in the same year. 21.5 per cent of maternal deaths were caused by eclampsia and pueperal sepsis. The effect of socio-economic factors on maternal health should also not be neglected. The highest incidence of illness is usually found in low-income groups stemming from low standard of living leading to low dietary levels, low level of medical expenditures etc. But the effects of frequent pregnancies and low income levels cannot be separated in this case since pregnancies occur frequently in these income groups. However, even a glimpse of the types of medical attention given to the women and of their nutritional status in the country as a whole, given the levels of income is a sufficient indicator of the extreme neglect of women in the most productive span of their life both absolutely and in relation to men in this nation leading to high rates of maternal morbidity and mortality. But any further elaboration of the phenomenon of sheer neglect of our female population in aspects of health should be based on a priori recognition that the extent of medical facilities available to the population as a whole, both men and women are very inadequate, which is somewhat evident from the fact that the availability of medical and para-medical personal falls far short of the requirments as can be seen in Table IX. The fact is that women are more adversely affected by the absence of a sound health infrastructure than the men, as by virtue of their reproductive function they require it most, keeping aside the fact of the differential medical facilities enjoyed by the two sexes in the patriarchal Indian society.

Table IX. Availability and Requirements (as per norms) of Medical and Para-Medical Personnel in 1971.

Class of Personnel	Personnel available in 1970[1]	Ratio of Nos. in Column 2 to population : 1971	Name of Requirement[2]	Estimated Requirement
(1)	(2)	(3)	(4)	(5)
Doctors	137964	3967	1 : 1000	547367
Nurses	77824	7033	1 : 500	1097734
Midwives	76239	7180	1 : 4000	136842
Auxiliary Nurse Midwives	26233	20865	1 : 1000	547367
Health Visitors	4283	127800	1 : 5000	109473
Dentists	5485	99793	1 : 4000	136842

Note : 1. The number of personnel of different categories for the year 1970 is taken from Medical, Nursing and Dental Councils of India. The information with them relates only to States. In Union Territories such councils are not formed hence the total figures of personnel are marginally on the lower side.

2. The norms regarding requirements of personnel are based on the ratios which have already been reached by U. K. prior to 1968-69.

Source : United Nations Children's Fund, South Central Asia Region : **Statistical Profile of Children and Youth in India.** Table 25, p. 28, prepared for the UNICEF by the Institute of Economic and Marketing Research, New Delhi, June 1972.

The implications of the information contained in Table IX become much more serious when we consider the Sample Registration System data relating to the types of medical attention given at birth which have an important bearing on maternal health. According to SRS data, in rural India in 1969, only 13.6 and 12.9 per cent of the total births received institutional and trained practitioners' attention respectively while rest of them were looked after by untrained practitioners and others as can be seen in Table X.

Table X. Per cent distribution of still births by types of medical attention at birth in rural India, SRS, 1968 and 1969 (unweighted).

		Type of medical attention at birth*				
	Year	Institutional	Trained Practitiooners	Untrained Practitioners	Others	Total
(Pooled estimates of Andhra Pradesh, Assam Gujrat, Haryana, Jammu & Kashmir, Kerala, Maharashtra, Mysore, Punjab, Rajasthan, Tamil Nadu & Uttar Pradesh)	1968	13.0	12.3	47.6	27.1	100.0
	1969	13.6	12.9	47.1	26.4	100.0

Source : SRS, Analytical Series No. 1 of 1971, p. 25, "Infant Mortality in India".

*Enumerators events only.

The National Sample Survey (NSS) data inspite of their varying coverage of area and population in the different rounds, indicate clearly the lack of proper medical attention received by infants and mothers in India in the early 60s. For example, NSS in its 19th round, 1964-65, reported that in the rural areas only 9 per cent of births were attended by trained dai or midwife and qualified nurse or physician and no medical advice was at all sought in 17 per cent of all deaths reported in the rural areas and 12 per cent of the same in in the urban areas, as can be seen in Table XI A and XI B.

Table XI A. Percentage distribution of births by type of attendance and sector : All India Households, NSS 19th Round 1964-65.

Sector	Untrained dai	Trained dai or midwife	Qualified nurse or physician	Relatives and others	Ne. attendance	All types
Rural	48.90	4.10	4.71	38.19	4.10	100
(Number of sample births)	(14350)	(1236)	(1439)	(10512)	(1036)	(23573)
Urban	33.04	15.71	30.42	18.79	2.04	100
(Number of sample births)	(4905)	(2219)	(4639)	(2464)	(271)	(14498)

Source : National Samlpe Survey : **Vital Rates in India,** No. 177, p. 82.

Table XI B. Percentage distribution of deaths by type of attendance and sector : All India Households, NSS 19th Round.

Sector	Untrained dai	Trained dai or midwife	Qualified nurse	Physician	Persons other than registered practitioner	No. medical consultation	All types
Rural	10.30	0.56	1.35	21.37	49.76	16.67	100
(Number of sample deaths)	(1043)	(60)	(130)	(2120)	(4689)	(1523)	(9565)
Urban	9.04	1 22	4.44	37.66	35.60	12.05	100
(Number of sample deaths)	(322)	(44)	(160)	(1376)	(1165)	(396)	(3463)

Source : Same as in Table XI A.

The attendance of the majority of the births by untrained personnel both in the rural and urban areas stems from the utter lack of a proper health infrastructure in the nation, extreme poverty of the masses leading to their inability to pay for skilled medical services, catering to the needs of the few economically fortunate ones, general apathy of the society and the households towards the health of the woman who is not usually the breadearner in the family (for example, in Uttar Pradesh, only 35.5 per cent of the beds in the medical institutions were for females in 1968), ignorance about the existing medical facilities in the given locality and the practice of having delivery in own premises for example, the National Sample Survey in its 19th round reported that in the rural areas 87 per cent of the births occurred in the own premises and 3 per cent occurred in the hospitals, maternity homes or other medical institutions. The comparable figures for the urban areas were 60 and 30 per cent respectively. Such rural-urban differential in the per cent distribution of births by place of birth arises mainly from the differential availability of the medical facilities in the two areas. Besides frequent pregnancies and lack of proper medical attention, maternal health also gets adversely affected by the malnutrition, a characteristic feature of the low income countries. According to Leela Iyengar, cereals' intake of pregnant women in India was just 276 g. against the recommended one of 400 g. while the intake of leafy vegetables was 8 g. against the recommended amount of 150 g. during the '60s. The Annual Report of Nutrition Research Laboratory, 1965-66 reveals that milk and milk products' intake of nursing mothers (vegetarian) was 23 g. against the recommended amout of 325 g. Against caloric requirement of 2500 and 2900 for pregnant and nursing mothers respectively, their actual intakes of calories were 1440 and 1425 respectively (Kulkarni 1975). Such malnutrition when coupled with frequent pregnancies can easily lead to severe anaemia which is one of the most important causes of maternal deaths in India.

The extremly high rate of maternal deaths coupled with a high infant mortality rate more adverse to females than to males in this country, can explain the phenomenon of persistently high sex ratio to a large extent but cannot explain the continuing increase in the same during the past seven decades for which we have reasonably accurate census' informations. The 50s and 60s in this country have been characterized by planned efforts to achieve rapid economic development with an adequate emphasis on the growth of infra-structure of health and education. The growing medical facilities coupled with some economic betterment have led to a perceptible decline in the general mortality rate of both the sexes. Infant mortality rate for registration areas declined from 215 (per 1000) during 1900-1905 to 161 during 1941-1945 (Sample Registration System, 1971), subject to the constraint of erraneous and limited data. Thus we can safely conclude that the onset of 40s was marked by a decline in infant mortality rate which fluctuated at a very high level before and continued to decline further in the ensuing decades (in 1971, the infant mortality rate was 131/1000). Such decline affected favourably the expectation of life at birth of both the sexes. The decline in maternal mortality rate has affected favourably the expectation of life of females. For example, the expectations of life at birth for males and females which were reported to be 26.3 and 24 years respectively in 1901 increased to 41.9 and 40.6 years in 1961 for males and females respectively. This implies that though longevity has increased considerably for both the sexes during the past decades, the relative increase in the same has been more in the case of males than in the case of females as can be seen in Table XII.

Table XII. Per cent increase in the expectation of life at birth in India: 1901-1967 (Increase or decrease over 1901)

Year (1)	Male (2)	Female (3)	Difference between (2) & (3) (4)
1901	—	—	—
1911	—4.2	—2.1	2.1
1921	N.A.	N.A.	—
1931	14.0	10.8	3.2
1941	N.A.	N.A.	—
1951	37.7	32.1	5.6
1961	77.5	69.2	8.3
1967 SRS	108.5	101.3	7.2

Source : Sample Registration System : SRS, Vol. VIII, No. 1, Registrar General Ministry of Home Affairs, New Delhi, Table 2, (April 1974), p. 30.

The differential rate of increase in the expectation of life at birth of the two sexes in favour of the males is primarily responsible for the increasing sex ratio in

India and so long as this advantage is retained by the male population, this trend will continue, to exist. According to the revised report of the Expert Committee on Population, the expectation of life at birth of males and females would increase from 23.6 and 24.0 years in 1901 to 53.2 and 51.8 years during 1971-82 (Sample Registration System, 1974) respectively implying percentage increases of 125 for males and 116 for females during the same period over the levels observed in 1901. This implies that the relative difference between the expectations of life of the two sexes will not narrow down during the present decade and the sex ratio will most probably rise further during the same period.

Implications : Increasing sex ratio has two implications : one demographic and another social.

If the sex ratio remains favourable to males in a monogamous, tradition-bound society over a long period, then the birth rate is negatively affected. Secondly, in such a society, in the absence of sufficient number of females to match the males, many of the latter have to remain bachelors. This can have serious social implications like increase in the extent of illegal traffiking, increase in the rate of crimes and other types of violence. In other words, if the imbalance in sex ratio persist for a long time, social instability can easily be the characteristic feature of the future.

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Trends in Fertility in Urban and Rural Indian Population Groups

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Introduction

Of the three determinants of population growth, that is fertility, mortality and migration, it is believed that future population growth in the developing countries will depend on trends in fertility rather than those in mortality or in migration. To-day migration plays a negligible role in the population growth of most developing countries because of restrictive international regulations. The low levels of mortality already prevalent in many developing countries, make further declines difficult to achieve and when achieved are expected to be spread out over a longer period of time. When the population problem looms large and is likely to negate any gains in developmental efforts, the greatest concern has to be with the course fertility is likely to take in the future and this course would, of course, depend on the past and the present situation.

It is widely known that the fertility of Indian women is high, as in many other developing countries. At this point it is necessary to distinguish between the terms fecundity and fertility, as used in demographic literature. Fecundity refers to "the capacity......to participate in reproduction (i. e. the production of a live child), whereas fertility means actual reproductive performance" (United Nations, 195). While there is no direct measurement of fecundity, which is the potential level of performance of the population or the physical capacity for bearing children, fertility is measured on the basis of the number of live births. Two approaches are followed in this respect. The first approach considers the reproductive performance of a particular group of women during the complete reproductive period, which may be for about 35 years. The other approach depends on the reproductive performance of a group of women during one year.

Unfortunately, it is difficult to make firm statements about the exact level of the fertility of Indian women due to the paucity of data. The estimates made by different demographers are also found to differ. For the purposes of this paper, therefore, it is intended to present a broad picture of the fertility of Indian women with the intention of understanding the situation, rather than getting involved in the controversies regarding different estimates. For illustrative purposes, estimates based on the data made available through the following sources are used : the Census, the National Sample Survey, the Sample Registration Scheme of the Registrar General's Office and the several fertility surveys carried out by different organisations.

Fertility Trends in India

The simplest and the crudest measure of fertility is the crude birth rate, which gives the number of live births in the population in one year per one thousand. It is a crude measure because it considers the entire population irrespective of its composition based on sex, age and marital status. Table I gives the birth rates and death rates for different periods, which-are acturial estimates based on census data. It can be seen that though there has been some decline in the birth rate from 1901-11, it is not substantial. From a birth rate of about 49 per thousand during 1901-11, the birth rate has declined to about 41 during the period 1961-71. During the same period, the death rate declined from about 43 to about 19. (It must, of course, be remembered that the figures for 1961-71 are estimated from one per cent sample data, and as the figures are based on improved methodology, they are not strictly comparable with the earlier figures. It has been pointed out that if no adjustment is made for under enumeration of certain younger age groups, as in the case of earlier figures, the comparative figures of birth and death rates for the decade 1961-71 would be 39.2 and 17.2 respectively.)

Table I. Birth and Death Rates since 1901-1971.

Decade	Rate by reverse survival method		By quasi-stable method	
	Birth Rate	Death Rate	Birth Rate	Death Rate
1901-11	49.2	42.6	52.4	46.8
1911-21	48.1	47.2	N.A.	N.A.
1921-31	46.4	36.3	50.8	40.4
1931-41	45.2	31.2	46.2	33.5
1941-51	39.9	27.4	43.1	30.0
1951-61	40.9	22.0	40.4	20.9
1961-71*	41.1	18.9	40.0	17.8

*Provisional. Estimated from one per cent sample data.

Source : Government of India, **Towards Equality : Report of the Committee on the Status of Women in India**, New Delhi : 1974, p. 26.

Though the birth rates appear to have declined over the years, when another measure of fertility, that is the gross reproduction rate, is considered, only a marginal decline from 1951-60 to 1961-70 is exhibited. (The gross reproduction rate gives the number of daughters a woman would have at the end of her reproductive period, if she went through a fixed fertility schedule, following the age specific fertility rates for different age groups.) It has been pointed out by Rele and Sinha (1973): "Hence it appears that a major part of the decline in the crude birth rate from 1951-60 to 1961-70 is due not to the change in the fertility of women but to the change in the age, sex and marital status composition, which was more favourable for a lower birth rate in 1971 compared to 1961." In support of this statement, they illustrate how the percentage of currently married women among women in the reproductive ages 15-44, the percentage of women in the reproductive ages 15-44 to all women, the sex ratio (number of females per 1000 males) of the population and the percentage of currently married women in the reproductive ages 15-44 to the total population were all lower in 1971 than in 1961 (Table II) They, (Rele and Sinha, 1973) however, go on to point out, "While comparison of the gross reproduction rates for the two decades of 1951-60 to 1961-70 shows little change in the level of fertility, there is some evidence of decline during the latter half of the last decade," (that is 1966-70).

Table II. Age, sex and marital status distribution in 1961 and 1971.

	1961	1971
a) The percentage of currently married women among women in the reproductive ages 15—44	85.8	84.5
b) The percentage of women in the reproductive ages 15—44 to all women	43.2	42.4
c) The sex ratio (number of females per 1000 males) of the population	941	930
d) The percentage of currently married women in the reproductive ages 15—44 to total population	18.0	17.3

Source : J. R. Rele and U. P. Sinha, "Birth and death rates in India during 1961-70—A census analysis", **Demography India**, Volume II, Number 2, December 1973, p. 276.

Further evidence also suggests that in recent years there has been some decline in the birth rate, which could be indicative of extension of the decline set in since 1966. The estimates of the Sample Registration Scheme of the Office of the Registrar General has indicated that the birth rate in 1969 was 37.6 and has come down to 36.6 in 1972 (Govt. of India, 1974). The estimates made on the basis of the performance of the family planning programme in terms of acceptors of different methods of family planning and the resulting number of births prevented, give a birth rate of 35.0 (provisional) for 1974-75, as compared to the estimate of 36.6 for 1972 given by the Sample Registration Scheme (Dept. of Family Planning, 1975).

Reasons for High Fertility : Though demographers may disagree in their estimates of the birth rate or in other measures of fertility, and about the extent of the declines in these measures in recent times, the fact remains that the fertility of Indian women has been and is still on the high side. An understanding of the socio-cultural environment in which reproduction takes place indicates some of the reasons for such a situation. There is no doubt that children will always be valued, not only as economic assets in a predominantly agricultural society like ours, or for the affectional needs of the parents that they fulfil, but for several other reasons. As pointed out by Blake (1965) "they are the instrumentalities for achieving virtually prescribed social status ('mother', 'father),' the most exclusive avenues for feminine creativity and achievement and the least common denominator for community participation."

Concerning the motivations of women for high fertility, it must be remembered that in a traditional society like ours, child-bearing itself restores prestige on the wife, and a childless woman is even looked down upon. Sociologists have observed that the new daughter-in-law in the Indian family is accorded her rightful status only after she gives birth to a child, preferably a son. The Indian woman knows and accepts the principle that she will be looked after and protected in childhood by her father, in adulthood by her husband and in old age by her sons. Sons are, therefore, important to her and she strives to have them. In the process, she may keep trying for a son, inspite of having several daughters. The importance of the son, for liberating the soul of the parents by lighting the funeral pyres of the parents, also makes it imperative for the parents to crave for a son. It is worth noting that even a daughter is wanted, because of the **punya** the parents accumulate by performing **kanyadana**.

Urban fertility lower than rural fertility ? It is normally expected that fertility would be lower in the urban than in the rural areas. There are several reasons for such an expectation, and these can be briefly touched upon at this point (United Nations, 1973). In the urban areas, the economic usefulness of the child to the parents is limited. On the contrary, each additional child becomes a liability as he has to be educated and the cost of bringing up a child in urban areas is higher than in the rural areas. In the urban areas, the mother has the opportunity to take up several extra-familial roles and, therefore, does not look to child-bearing and child-rearing as a major source of ego extension and satisfaction. The burden of additional children has to be borne by the nuclear family in the urban areas, whereas the joint family in the rural areas absorbs all the children born within its fold. In the rural areas, the pressure to conform is also greater and any deviation from expected behaviour, in this particular case having a large family, is frowned upon In the urban areas, mortality declines earlier and more children are likely to survive than in the rural areas. An urban woman can give birth to fewer children and expect them to survive, whereas the high infant mortality rates in the rural areas prompt couples to have a large number of children in the hope that at least a few would survive to adulthood. Even when infant mortality rates decline, there is always a lag between the actual decline and the perception of the people and couples continue to go in for large families even when it is not necessary to do so. The urban areas are usually characterized by securalization, secondary group associations, increased segmentation of roles and poorly defined norms. Opportunities for the education and employment of women help to improve the status of women and greater exposure to mass media widens their horizons, making them more amenable to the acceptance of new ideas and values.

In addition, the higher age at marriage for women in urban areas, may also have demographic implications, though it is doubtful whether higher age at marriage by itself (unless it is particularly high as in the case of Ireland) would lead to much reduction in fertility, unless some conscious effort is made to control fertility through contraception. It is, however, expected that with a higher age at marriage, women would have more opportunities for education and employment, would be more mature while entering marriage and, therefore, would be more likely to subscribe to the idea of voluntary parenthood, with implications for their fertility performance.

The Situation in India

What is the situation as far as the fertility pattern of urban and rural women in India is concerned ? The actual reproductive behaviour of Indian women indicates that the expected rural-urban differentials in fertility are practically non-existent and have started making their appearance only in recent years. Davis (1961) found that the child-woman ratio showed only small rural-urban differentials in fertility in 1951. Rele, however, writing in 1972 and considering the period after 1951 has illustrated how urban fertility has tended to be lower than rural fertility in the recent past when the following indices are used : child-woman ratio, marital child-woman ratio, the crude birth rate, the adjusted birth rate and the total fertility rate. He optimistically points out, "This may be indicative of an incipient decline of fertility in India" (Rele, 1972).

The birth rates for rural and urban areas for the period 1969-72, according to the Sample Registration Scheme also indicate some rural-urban differentials (Table III). For instance, the birth rates for rural and urban areas in 1969 were 38 8 and

32.6 per thousand respectively. The corresponding figures for 1972 were 38.4 and 30 5. These figures also highlight the fact that though there has been some decline in the birth rate in the urban areas, the decline in the rural areas is negligible (Govt. of India, 1974).

Table III. Birth rates in India according to the Sample Registration Scheme data, 1969-72.

Year	Rural	Urban	Total
1969	38.8	32.6	37.6
1970	38.9	29.7	36.8
1971	38.9	30.1	36.9
1972	38.4	30.5	36.6

Source : Same as for Table I, p. 26.

The fact that the fertility of rural women is high is brought out by several studies. In rural India, in 1969, according to the Sample Registration Scheme, the average number of children born to women in the age group 40-44 was 6.4, which can be considered to be the completed family size of rural women. It is also indicated by the data that by the time the rural woman reaches the age of 35, she has already had about 5 children (Govt. of India, 1974) (Table IV). Another indicator of the fertility pattern of rural women is the distribution of births taking place during one year by their order of birth. It is revealing that of all the births which took place in rural India in 1969, according to the data of the Sample Registration Scheme, 45 per cent were either the fourth order or above. When the birth order of five and above was considered, this percentage was 30.5 (Govt. of India, 1974) (Table V). These percentages indicate the extent of the higher order births in rural areas, which if avoided would change the picture of the fertility pattern of Indian women considerably.

Table IV. Average number of children born alive to current mothers by age groups for Rural India, 1969.

Age group	Average number of children
15—19	1.3
20—24	2.1
25—29	3.5
30—34	4.8
35—39	5.8
40—44	6.4

Source : Same as for Table III, p. 28.

Table V. Percentage distribution of the live births by birth order for Rural India, 1969.

Birth Order	Percent
All orders	100.0
1st	20.5
2nd	18.1
3rd	16.4
4th	14 5
5th	11.6
6th	8.2
7th	5.3
8th	2.8
9th	1.5
10th	1.1

Source : Same as for Tables I, III and IV, p. 29.

It can be expected that urban-rural differentials will become conspicuously evident only when urban Indians truly adopt the urban way of life. To-day, though they live in urban areas, most of them maintain their rural ties and cling to their roots, move in their own language group and live close to their own caste and family group. The 'urban mentality' with rising aspirations and expectations, which could be responsible for declining family size, is sadly lacking. With reference to the status of women, such an urban mentality could mean the acceptance of women by men as equal partners in life and the recognition of an improved self-image by women with their acceptance of alternate roles of self-expression and self-development rather than merely those of childbearing and childrearing.

Education of Women and Fertility ; Ample evidence is available in India, as in many other countries, to indicate that more important than urban or rural residence, the educational status of wife determines her fertility performance and that the educational status of the wife is negatively associated with fertility. Such evidence is generally available in surveys conducted in the urban areas as only in such areas it is possible to find women with higher educational attainment.

The Mysore Population Study indicated that in Bangalore city, the average number of children born to ever-married women above the age of 45 was 5.4 for illiterate women, whereas it was 3.9 for women with high school or college education. Though this difference was partly due to the higher age at marriage for those with high school or college education, these differences persisted, though to a lesser extent, even when the averages were standardized by age and duration of marriage (United Nations, 1961). Similarly, it was found in the Sixteenth Round of the National

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Sample Survey held in 1960-61, that among women who were 47 years old and over, the total completed fertility varied inversely with educational attainment. Illiterate women or those with only primary education had an average of 6.6 live births; those who had a middle school education averaged 5.0 live births; those who had completed high school education had 4.6 live births; and those who had some university education had only 2.0 live births.

The role of the educational status of the wife was also brought out when an attempt was made to study differentials in marital fertility by former residence of 7,872 currently married women in Greater Bombay in 1966. The standardized average number of children ever born by former residence was found to be 3.0 for non-migrants, 2.90 for urban migrants and 3.42 for rural migrants. It has been pointed out that "the variable that has emerged as the most influential in creating fertility differentials is of wife's education, which is shown to have a negative association with fertility. Wife's education explains to a great extent the fertility differentials by former residence" (Rele and Kanitkar 1974).

While commenting on the usual association between the educational status of the wife and fertility, Cool (1973) points out, "It is recognized that many other factors were at work, in addition to education and that it is not possible to say with precision what proportion of fertility differentials related to education are exclusively a result of education itself, but a recent study has shown that over one-third of the total variance in fertility in a number of countries, is the result of education and that education was four times more significant than a combination of all other variables which were measured". Here again, while understanding the interrelationship between educational attainment and fertility, it is important to remember that "It is not higher education **per se**, but its association with factors such as openness to new ideas, higher socio-economic status and standards of living, exposure to an urban environment, and a greater range of options and interests outside the home that is responsible for the apparent influence of one on the other" (United Nations, 1974).

Religion and Fertility : Another point of interest while studying fertility patterns of different groups is whether the fertility of different religious groups differs. Several local surveys have brought out that by and large Muslims have higher fertility than Hindus (Agarwala, 1973). Even in Greater Bombay, analysis of approximately 50 per cent of the births registered during 1960, revealed that Muslim women recorded the highest average parity. Their standardized average parity per 100 mothers was 366, whereas it was 339 for Hindu mothers, 306 for Christian mothers and 195 for Parsee mothers (El-Badry, 19[illegible]7).

Apart from the fact that a large proportion of Muslim women are married and in the reproductive ages compared to Hindu women, probably because there is no restriction on widow-remarriage, the lower socio-economic status of the majority of the Muslims may also be considered to be a contributing reason for their higher fertility. In this connection, it is worth noting that "it has been found in a study carried out in Bombay that the higher socio-economic group Muslims have the same or even lower fertility than the higher-class Hindus and the fertility of lower-class Muslims is only a shade higher than their Hindu counterparts" (Agarwala, 1972). It, therefore, appears that with the narrowing of the differences in socio-economic status, the important among these being the educational status of women, these differentials in fertility should become less or even disappear.

Summary and Conclusions

A study of the fertility of Indian women is important because of the three determinants of population growth, that is fertility, mortality and migration, the present and future course of fertility will determine the future population growth. The fertility of Indian women is known to be high as is evident by various indicators. Over the years, though the declines in the death rates have been substantial, the declines in the birth rates have been of a minor nature. Since 1966, here is definite evidence of the beginning of a decline.

Urban-rural differentials in fertility were not evident to any great extent till 1951, but after that period the differentials have started manifesting themselves. Fertility of women in the rural areas continues to be high with women having between 6 and 7 children by the time they come to the end of the reproductive period. The proportion of higher order births in the rural areas is also substantial. Greater urban-rural differentials in fertility can be expected only when the urban people also adopt an urban mentality.

The educational status of women is found to have a very clear negative association with fertility performance as is evidenced in several surveys carried out in different parts of the country.

Though the fertility of Muslim women is found to be higher than that of other religious communities, there is evidence to suggest that this difference may be due, by and large, to the low socio economic status of this group and the fertility differentials are likely to diminish or even disappear, once the differences in socio-economic status are narrowed down. Here again, the education of women may be expected to play an important role in improving her status.

A study of the fertility patterns of women belonging to different groups in India highlights the importance of improving the status of women, by concentrating on improving their educational status, if the fertility patterns are to be influenced in any significant manner. The proportion of higher order births in rural areas indicates that if such births could be avoided, fertility would decline. Education of women would make them aware of the problems of excessive fertility, help them to cultivate a better self-image and induce them to seek alternate roles rather than aiming at fulfilment only in childbearing and childrearing. Status in society would then be accorded to them not only as wives and mothers but also as individuals contributing to their own development as well as that of their family, their community and their country.

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Maternal Mortality in India and its Prevention

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Introduction

Maternal mortality is a very sensitive index which directly reflects upon the socio-economic status of any country, and is a vital problem facing the developing countries. Its reduction and prevention requires a concentrated effort on a national level **viz.** (1) raising the standard of living, and socio-economic status; (2) orienting medical education in the right direction; (3) training of paramedical staff; and (4) ideal ante-natal, intra-natal and post-natal care are the important facets in this problem. Family Planning is the key note to the betterment of the socio-economic status of any family.

With a population of almost 600 million, a birth rate of 36/1000, and maternal mortality rate of 3/1000, over 54,000 materal deaths occur annually in our country.

Definition : In accordance with the F. I. G. O. International Committee, maternal deaths is defined as the death of any woman dying of any cause during pregnancy or within 42 days of termination of pregnancy, irrespective of the duration and site of pregnancy.

Maternal mortality ratios/rates : In order to have information on the number of maternal deaths, the following ratios are used :

(1) Total Maternal Mortality Ratio is the number of maternal deaths (direct, indirect, and non-obstetric), per 10,000 live births, the latter being defined as the birth of a live born infant of weight 1,000 g. or more, and in the absence of weight, an estimated duration of 28 weeks gestation (calculated from the first day of the last normal menstrual period).

(2) Obstetric Death Ratio is defined in the same manner as previous one, but including only the number of direct and indirect obstetric deaths.

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Classification of Maternal Deaths according to F. I. G. O. Committee, (Alvarez Bravo, 1969) :

I. (a) Obstetric Maternal Death is that resulting from direct and indirect obstetric causes.

   (i) Direct obstetrical death is that resulting from obstetric complications of the pregnancy state, labour, puerperium from omissions, interventions and incorrect treatment.

   (ii) Indirect obstetrical death is that resulting from previous existing disease developed during pregnancy and aggravated by the physiological effects of pregnancy, e.g. heart disease, pulmonary disease and cardio-vascular accidents.

(b) Non-obstetrical maternal death is that resulting from accidental or incidental causes not related to pregnancy.

II. (i) Preventable maternal deaths (Avoidable deaths).

(ii) Probably non-preventable maternal deaths (Unavoidable deaths).

(iii) Unexplained deaths.

III. Late Maternal Deaths—where death occurs 6-12 months after puerperium from conditions for which her state of pregnancy was primarily responsible e.g. chorionic epithelioma, puerperal anaemia.

Maternal Care in India

Maternal and Child Health Services owe a debt of gratitude to the devoted and untiring efforts of voluntary organisations that were established chiefly during the later half of the 19th century.

1. Countess Dufferin Fund (1860).
2. Victoria Memorial Scholarship Funds (1903).
3. Lady Chelmsford All India League for Maternity and Child Welfare (1920).
4. Red Cross Society—Maternal and Child Health Bureau (1920).
5. The Bhore Committee (1946)-

Two decades of planned development: The Government of India undertook Five Year Development Plans.

(i) The First Five Year Plan emphasised the needs of rural areas where almost 80 per cent of the total population lives. In the rural areas only about 7 per cent of the deliveries take place in institutions, the rest of the mothers being delivered in their homes, mostly by untrained personnel with the attendant high maternal morbidity and mortality.

(ii) The Second Five Year Plan—Maternity and Child Welfare service was made an integral part of the primary health units. Three thousand primary health centres were established. The existing facilities for maternal and child health are (Sharma **et al**, 1975) :

(a) Physical facilities (Table I)
(b) Manpower Resources (Table II)
(c) Training facilities (Table III)

Table I. Physical facilities.

Type of Institutions	Number 1950—51	Number 1965—66	Number 1973-74
Primary Health Centre	—	4,796	5256
Sub-centres	—	13,072	33048
M. C. H. Centres	1,700	8,900	8492
Maternity Beds	10,000	45,077	47606
Children beds	N.A	8,393	9353

Table II. Manpower resources.

Category	1950-51	1965-66	1970-71
Doctors	56,000	86,000	1,15,723
Nurses	15,000	45,000	71,000
Auxiliary-Nurse-Midwives/ Midwives	8,000	36,000	57,000
Lady Health Visitors	521	4,200	5,933

Table III. Training facilities .

Category	*1950-51* No. of Schools	*1950-51* No. of annual admissions	*1965-66* No. of Schools	*1965-66* No. of Annual admissions	*1973-74* No. of Schools	*1973-74* No. of annual admissions
MEDICAL						
Medical Colleges	30	3,500	87	10,520	106	11,500
NURSING						
Certificate in Nursing	NA	NA	245	5,565	260	19,121
B. Sc. Nursing	NA	NA	9	195	9	185
Lady Health Visitors	9	92	19	1,186	19	1,641
Auxilary Nurse Midwife	NIL	NIL	273	5,500	305	7,100
Public Health Nurse	NIL	NIL	6	120	6	120

World Statistics on maternal mortality varies considerably because the diagnostic criteria and coding differs from country to country. India occupies a low position in this context (Registrar General of India, 1972) (Table IV).

Table IV. Maternal mortality in different countries.

COUNTRY	YEAR	M. M. RATE
U. K.	1968	2.9
U. S. A.	1965	3.2
HONG KONG	1966	4.4
SINGAPORE	1966	5.0
TAIWAN	1966	7.2
MALAYSIA	1966	20.0
PHILIPPINES	1965	21.0
INDIA	1968	57.3

Accurate data regarding maternal mortality in India is not available due to inherent qualitative and quantitative deficiencies in the registration of vital events. Until such time as every death is certifiable by a competent authority, selectivity in the study of maternal mortality cannot be overcome. In India, of the deaths reported by the rural death recording system, 50 per cent are via unauthorised sources—thereby indicating a high magnitude of avoidable factors.

The maternal mortality rate in India during 1966-70 is 5.9/1000 live births (Sen Gupt a, S. K., 1972). However, it varies from State to State (Table V).

Factors influencing maternal mortality :

1. Age (Table VI)
2. Parity (Table VII)
3. Socio-economic status (Table VIII)
4. Marital status—total illegitimacy rate 4 per cent
5. Antenatal, Intranatal and postnatal care.

Table V. Maternal mortality in India.

NAME OF THE STATE	YEAR	M. M. RATE
RAJASTHAN	1965	6.9
MADRAS	,,	4.1
MADHYA PRADESH	,,	3.9
ASSAM	,,	2.9
ORISSA	,,	2.5
MAHARASHTRA	,,	2.2
WEST BENGAL	,,	2.2
ANDHRA PRADESH	,,	2.0
GUJARAT	,,	1.6
J & K	,,	1.6
U. P.	,,	1.4
PUNJAB	,,	1.1
BIHAR	,,	1.0
MYSORE	,,	0.5
DELHI	,,	0.4

Table VI. Maternal mortality in relation to age (Pandya et al 1969).

Age	
18—24 yr.	6.72
Above 24 years.	83.26

Table VII. Maternal mortality in relation to parity (Pandya et al 1969).

PARITY	1—3	19.08
	4& above	80.58

Table VIII. Maternal mortality in relation to socio-economic Status (Pandya et al 1969).

Poor socio-economic group	36.04%
Middle socio-economic group	57.24%

Of the 13 million women who deliver in this country every year, over 80 per cent receive no antenatal care thus resulting in a high maternal and perinatal mortality. Both, the quality and quantity of antenatal care influence mortality. The overall high mortality amongst the unbooked cases is apparent in Graph 1. Unbooked cases have a high mortality rate owing to the presence of complications **viz.** anaemia, hypoproteinemia, avitaminosis, toxaemia and associated medical disorders. The main causes of mortality following caesarean section in infected cases are peritonitis and post operative shock. Causes of deaths during pregnancy, labour and puerperium as reported by Mukherjee (1969) are given in Tables IX, X and XI.

Table IX. Deaths during pregnancy.

CAUSE	YEAR 1963	YEAR 1964
Toxaemia	17.4%	14.8%
Haemorrhage	8.0%	7.7%
Anaemia	2.2%	7.2%
Disease of Genito-Urinary Tract	1.1%	0.5%
Other complications	12.7%	4.4%
Abortions without complications	3.4%	5.2%
Abortions with other complications	6.0%	1.7%

Table X. Deaths during labour.

CAUSE	YEAR 1964
Haemorrhage	12.2%
Prolonged Labour	5.2%
Instrumental and operative delivery.	4.3%
Trauma—Perenial Lacerations —Rupture uterus	2.1%

Table XI. Deaths during puerperium.

CAUSE	YEAR 1964
Sepsis	3.5%
Puerperal Eclampsia and other toxaemias	1.8%
Mastitis and disorders of lactation	1.7%
Pulmonary Embolism	1.0%
Urinary Infections	0.7%
Phlebitis	0.6%
Puerperal Pyrexia	0.6%

Indian women of the poor socio-economic strata—anaemic and malnourished are particularly vulnerable to the cumulative deleterious effects of pregnancy, post-partum blood loss and lactation. Probably, a large proportion of our maternal deaths can be prevented by convincing the women to attend antenatal clinics regularly from as early a period of pregnancy as possible or having fallen ill, to seek timely medical aid.

Prevention

Maternal Mortality Committee : In order to have a comparative study and scientific analysis of all factors involved in maternal deaths, the first maternal mortality committee was formed at Canada in 1925 and gradually spread all over the world by 1962 These committees are International, National, Regional and Institutional.

The chief functions of these committees are :

1. Full scientific analysis of the cause of every maternal death with rigid adherence to ethical and legal principles.
2. Determination of existence and nature of preventable factors, if any.
3. Objective and impersonal report and dissemination of knowledge gained.
4. Education of all medical and non-medical personnel connected with obstetrics as well as the public.
5. Preparation and publication of statistics on maternal mortality concerned with its jurisdiction.

Community Service : The comprehensive health services programme being built up for the rural areas will contribute to a significant reduction in maternal mortality (Graph 1) and morbidity in India. In addition, it will reduce perinatal mortality by improving the birth weight of the babies (Graph 2). In order to man these expanding services, training of health personnel in particular, the Auxillary Nurse Midwife (ANM) forms an integral part.

In order to reduce the maternal mortality atleast the ANM should render antenatal, intranatal and postnatal care to mothers in the community. ANM should receive refresher courses in keeping with the recent advances in the field of medicine—to enable her to detect the high risk pregnancy cases and refer them to the Primary Health Centre or District Hospital. The Medical Officer Incharge of a Primary

Health Centre or District Hospital should himself be aware of the high risk pregnancy group of patients (Table XII).

Table XII. High risk pregnancy.

History of Perinatal Deaths
Habitual Abortions
Pre-Eclamptic Toxaemia
Diabetes and Pre Diabetes
Heart Disease
Rh Incompatibility
Premature Births
Grand Multipara
Anti Partum Haemorrhage
Previous Caesarean

Orgnanisation of Flying Squads and Transfusion services to meet urgent emergencies at smaller centres and at the patients home will prove invaluable in a country like India.

A careful scrutiny of all maternal deaths, supported by autopsy, and discussion of the possible preventable factors in each case will go a long way towards reducing maternal mortality.

Anaemia is the common denominator in most of the maternal deaths in India, and a direct cause in 20 per cent. Eradication of poverty, chronic infections and infestations and improvement in diet are essential. In addition, effective family planning measures will help to prevent the rapid succession of pregnancies. This coupled with adequate antenatal and intra-natal care will help to reduce the mortality. Raising the socio-economic status as envisaged in 20 point programme will prove invaluable in reducing the country's maternal mortality and morbidity.

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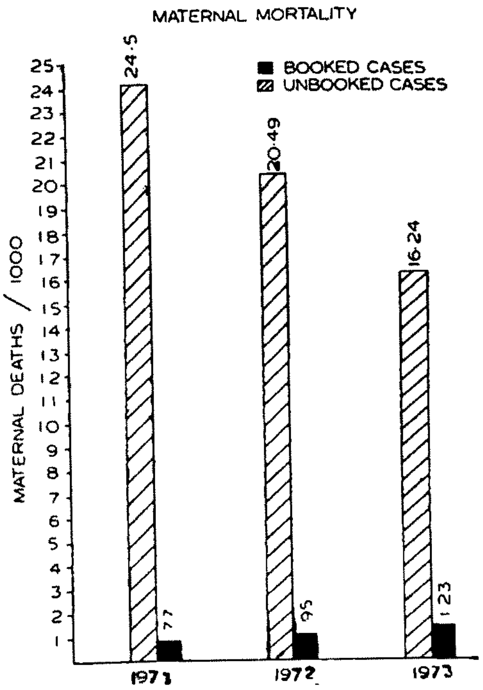
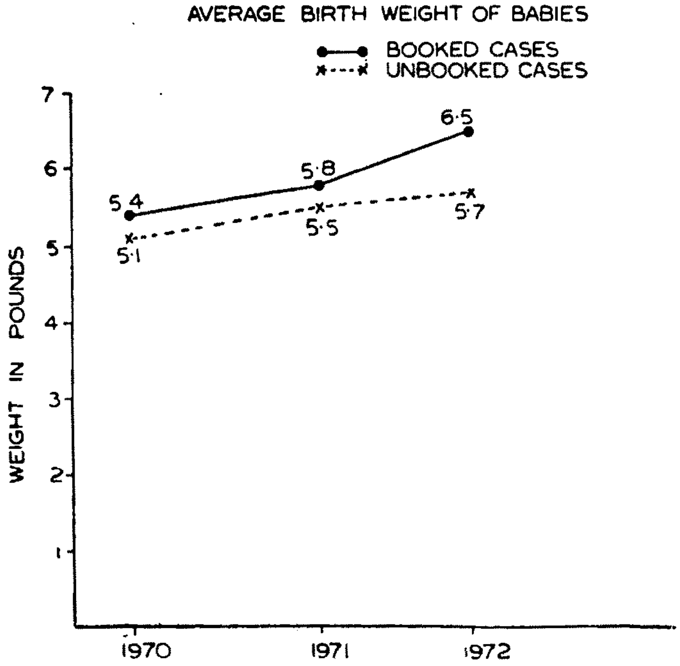
Graph 1.



Graph 2.



Ann Indian Acad Med Sci, 12, 4, Oct—Dec. 1976

Rapporteur's Report I

Report of Scientific Session I—Demographic Aspects

Chairman : Dr. C. Gopalan
Rapporteur : Dr. Prabha Malhotra

During the session three papers were presented :

(i) 'The Increasing Sex Ratio in India' by Miss A. Chatterjee.

(ii) 'Trends in Fertility in Urban and Rural Indian Population Groups' by Dr Asha A. Bhende.

(iii) 'Maternal Mortality in India and its prevention' by Dr. (Mrs.) V. Hingorani.

Miss Chatterjee in her paper 'The Increasing Sex Ratio in India' stressed the following :

That the increasing masculinity ratio (Males per 100 females) of Indian population during the past several decades is a curious phenomenon from the analytical point of view. Mainly three hypotheses have been put forward to explain such a phenomenon. The first hypothesis purporting to explain the masculinity of the population has been that the censuses under enumerate women to a greater extent than men. The second hypothesis asserts that the sex ratio in India is higher than the usual ones existent in the western countries due to the higher sex ratio at birth, in the former than in the latter. The available data for the same, however, do not support such a contention The third hypothesis attributes the same to the differential mortality in favour of the males in infancy and in the age group 15-45 years. The postnatal mortality rates of female infants are much greater than their male counterparts. This advantage to the females continues unabated till the age of 4 and then gradually the differences between the two sexes get narrower till the middle of the teen ages and again widens till the age of 34 years. Thereafter, the age specific death rates of females remain somewhat lower than the same of the males. The differential mortality rates of the two sexes in favour of the males in the age group of 15-45 years are caused by the prevalence of extremely high maternal mortality rates in India stemming from frequent pregnancies resulting in the increased incidence of hypertension, haemorrhage, anaemia, eclampsia and pueperal sepsis. The tendency towards high maternal mortality rates gets accentuated by the lack of medical facilities, nutrition and education. The high rates of female mortality stemming from high rates of maternal deaths and higher rates of mortality of females in infancy are the main causes of high sex ratio in India. However, the continuous rise in the sex ratio during the past seven decades has stemmed from the greater relative increase in the expectation of life of males than that of the females. If the males retain such advantage in the present decade as is expected by the expert Committee on population, then the sex ratio will register a further rise resulting in social instability characteristic of a society having an excess number of males over females over a long period.

Implications : Increasing sex ratio has two implications, one demographic and another social. If the sex ratio remain favourable to males in a monogamous, tradition-bound society over a long period, then the birth rate is negatively affected. Secondly, in such a society, in the absence of sufficient number of females to match the males, many of the latter have to remain bachelors. This can have serious social implications like increase in the extent of illegal trafficking, increase in the rate of crimes and other types of violence. In other words, if the imbalance in sex ratio persist for a long time, social instability can easily be the characteristic feature of the future.

Dr. Bhende in her paper on 'Trends in Fertility in Urban and Rural Indian Population Groups' has indicated that three detriments of population growth were important. Fertility, mortality and migration and of these she felt that the fertility of the Indian women is the most important criteria for determining the future population growth in the country. The fertility of Indian women is known to be high as is evident by various indicators. Over the years, though the declines in the death rates have been substantial, the declines in the birth rates have been of a minor nature. Since 1966, there is definite evidence of the beginning of a decline.

Urban-Rural differentials in fertility were not evident to any great extent till 1951, but after that period the differentials have started manifesting themselves. Fertility of women in the rural areas continues to be high with women having between 6 and 7 children by the time they come to the end of the reproductive period. The proportion of higher order births in the rural areas is also substantial. Greater urban-rural differentials in fertility can be expected only when the urban people also adopt an urban mentality.

The educational status of women is found to have a very clear negative association with fertility performance as is evidenced in several surveys carried out in different parts of the country.

Though the fertility of Muslim women is found to be higher than that of other religious communities, there is evidence to suggest that this difference may be due, by and large, to the low socio-economic status of this group and the fertility differentials are likely to diminish or even disappear, once the difference in socio-economic status are narrowed down. Here again, the education of women may be expected to play an important role in improving her status.

Implications : A study of the fertility patterns of women belonging to different groups in India highlights the importance of improving the status of women, by concentrating on improving their educational status, if the fertility patterns are to be influenced in any significant manner. The proportion of higher order births in rural areas indicates that if such birth could be avoided, fertility would decline. Education of women would make them aware of the problem of excessive fertility, help them to cultivate a better self-image and induce them to seek alternate roles rather than aiming at fulfilment only in childbearing and childrearing. Status in society would then be accorded to them not only as wives and mothers but also as individuals contributing to their own development as well as that of their family, their community and their country.

Dr. Hingorani in her paper on 'Maternal Mortality in India and its prevention' has indicated that there is a wide variation in maternal mortality prevailing not only in the different countries of the world but even within the country. The matenal mortality in the country differs widely with a rate of 6.9 in Rajasthan to a low figure of 0.4 in Delhi. It was further brought out that the causes of maternal mortality are preventable and efforts should be made to work towards the low figure which some of the states in the country have been able to achieve.

The role of Maternal Mortality Committees at international, national and institutional level was stressed. These committees would help or assist in the scientific analysis of the cause of the maternal death with rigid adherence to ethical and legal principles. This would also assist in education of all medical and non-medical personnel connected with obstetrics as well as the public, ahd further help to prepare and publish statistics on maternal mortality.

In discussing community services, the impact of the comprehensive health services programme being built up for the rural area which assist to contribute to a significant reduction in maternal mortality and morbidity in India. This impact will also be observed through a reduction in the perinatal mortality by improving the birth weight of the babies. The need for training of health personnel in particular the Auxillary Nurse Midwife was emphasised. Dr. Hingorani emphasised the need for organisation of Flying Squads and Transfusion services to meet the urgent emergencies at the patient's home in a country like India. It was suggested that a careful scrutiny of all maternal deaths and discussion of the possible preventable factors in each case would go a long way towards reducing maternal mortality. Anaemia was found to be the common denominator in most of the maternal deaths in India and direct cause in 20 per cent of the cases calls for immediate action.

Implications : Maternal mortality is a very sensitive index which directly reflects upon the socio-economic status of any country, and is a vital problem facing the developing countries. Its reduction and prevention requires a concentrated effort on a national level **viz.**

1. raising the standard of living, socio-economic status as envisaged in 20 point programme will prove invaluable in reducing the country's maternal mortality and morbidity,
2. orienting medical education in the right direction,
3. training of paramedical staff, and
4. ideal antenatal, intranatal and post-natal care.

are the important facets in this problem. Family Planning is the keynote to the betterment of the socio-economic status of any family.

With a population of almost 600 million, a birth rate of 36/1000 and maternal mortality rate of 3/1000—over 54,000 maternal deaths occur annually in our country.

Scientific Session II

Nutrition and Health Aspects

Ann Indian Acad Med Sci, 12, 4, Oct—Dec 1976

Nutrition in Pregnancy and Lactation

Bhavani Belavady

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Reproduction is a very important and crucial phase in a woman's life. In fact, it had come to be believed that her life was not complete without having a baby. Even at the present time, pregnancy and nursing contribute much to the health, joy and happiness of women. They make heavy demands in terms of nutrients. Unfortunately, in our country, the proportion of women who go through these stressful periods with adequate preparation is small and we have got to concern ourselves with women of the low socio economic group who do not have even the basic necessities of life.

Pregnant and nursing women are one of the most vulnerable groups in a community and the National Institute of Nutrition has been concerned with this problem for a long time specially in relation to the nutritional status of women and the new born.

Pregnancy

The Table I gives the dietary intake of some of the important nutrients of pregnant women. It will be seen that the diet is deficient in all nutrients.

Table I. Nutrient intake in pregnancy.

	Net calories	Protein g.	Iron mg.	Calcium g.	Vitamin A I.U.
Recommended allowance	2,500	55.0	40	1.0	2,500
Daily intake*	1,815	44	18.2	0.4	800
Per cent deficit	43	33	55	80	68

*Source : Pasricha, S. 1957. **Indian J Med Res, 46** 605.

A normal healthy pregnant woman gains considerable amount of weight during pregnancy which is accounted for, by the growth of foetus in-utero, the growth of the accessory organs and tissues of the woman and deposition of fat, which is utilised after parturition to meet the demands of lactation, The body weight increase observed in Indian woman during pregnancy is shown in Table-II. The increase in well nourished women range around 10-12 kg. (Hytten and Leitch, 1971) as compared to the 6 kg. gain experienced by poor Indian women. The deficiency signs that are commonly seen among pregnant women are seen in the next table (Table III) and it will be observed that less than 40 per cent of the pregnant women are free from clinical signs of deficiency. If biochemical parameters of assessment of nutritional status were to be employed, the proportion of well nourished pregnant woman will be much less. The outcome of pregnancy is shown in Table-IV. Anaemia is one of the major problems. Much has been said about this problem and based on the investigations carried out at the Institute a prophylactic programme for the prevention of anaemia is currently in progress in many States. This problem is being dealt with in great detail by another participant at the symposium.

Table II. Weight increase (kg.) during pregnancy at four weekly intervals.

Term in weeks	12—16	16—20	20—24	24—28	28—32	32—36	36—40
Prime-gravidae	0.30	0.84	1.52	0.85	0.64	0.74	0.28
Multi-gravidae	1.10	1.12	1.46	.96	0.95	0.79	0.35

Source : Venkatachalam, P. S., Kalpakam Shankar and Gopalan, C. 1960. **Indian J Med Res 48,** 511.

Table III. Nutritional status of pregnant women of low socio economic group.

Apparently healthy women	34.0%
Anaemia (Haemoglobin<11.0 g/100 ml)	57.5%
Glossitis	13.1%
Angular stomatitis	11.5%
Paraesthesias	42·0%
Oedema of feet	2.8%

Source : Gopalan, and Rao, K.S.J., 1972, **Tropical Doctor 2,** 188.

Table IV. Course and outcome of Pregancy.

Abortion	5.9%
Miscarriage	1.6%
Albuminuria	4.2%
Albuminuria and oedema	4.2%
Eclampsia	2.5%
Still births	7.6%
Live births	84.9%
Maternal mortality	1.6%

Source : Gopalan, C. and Kamala S. Jaya Rao, 1972. **Tropical Doctor 2,** 188.

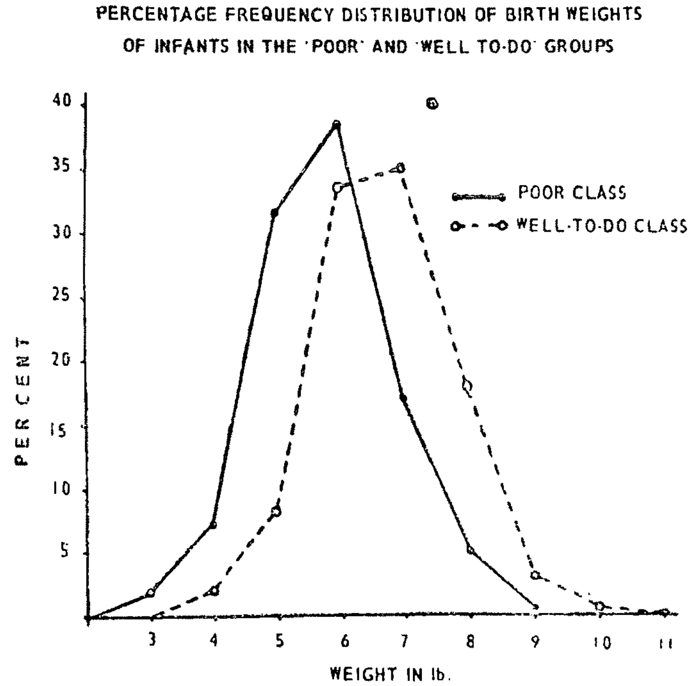
The birth weight of infants born to women from low socio-economic group is significantly low (Table V and Graph 1). The incidence of prematurity and low birth weights are high in this group. Some studies using functional parameters have demonstrated that a birth weight below 2.5 kgs. increases the risk of morbidity and mortality. Studies on the body stores of nutrients in these infants have indicated that these were low (Iyengar and Apte 1972).

Table V. Birth weight of infants in different economic groups.

	High socio-economic group	Low socio-economic group
No. of subjects	1753	2777
Mean birth weight	3182 g.	2810 g.
Immaturity (based on WHO standard)	13.8%	29.3%

Source : P. S. Venkatachalam. 1962. **WHO Bull 26** 193.

Graph 1 Distribution of birth-weights among low and high socio-economic groups.



PERCENTAGE FREQUENCY DISTRIBUTION OF BIRTH WEIGHTS OF INFANTS IN THE 'POOR' AND 'WELL TO-DO' GROUPS

Source : Varkki et al 1955, **Indian J Med Res 43**, 291.

Supplementation of diets with various nutrients individually or in combination have demonstrated favourable effects. Supplementations with iron and folic acid have proved successful in the prevention of anaemia (Iyengar and Apte, 1970). Calorie and protein supplementation even during last 4-5 weeks of gestation resulted in a significant increase in the birth weight of the infants as well as the increase in body weight of the pregnant women. The results are shown in Table VI. Vitamin-A brought about significant increase in the vitamin concentration in cord blood (Table VII).

Table VI. Effect of nutrient supplements on maternal weight gain and birth-weight of infant.

Group	Intake of Calories	Intake of Protein g.	Birth weight g.	Gain in maternal weight Kg.
Unsupplemented	1500	40	2704	0.35
Supplemented				
1	2400	60	3028	1.27
2	2400	90	3028	1.23

Source : Leela Iyengar. 1967. **Indian J Med Res 55,** 85.

Table VII. Serum concentrations ef carotene and vitamin A in neonates.

	Serum carotene (µg/100 ml)	Serum vitamin A (I. U. /100 ml)
Pregnant mothers (Third trimester)	99.0±6.70*	67.2±5.71
Neonates of mothers who received no vitamin A supplements	24.1±1.98	49.9±6.79
Neonates of mothers who received supplements of vitamin A	21.3±3.55	84.2±2.58

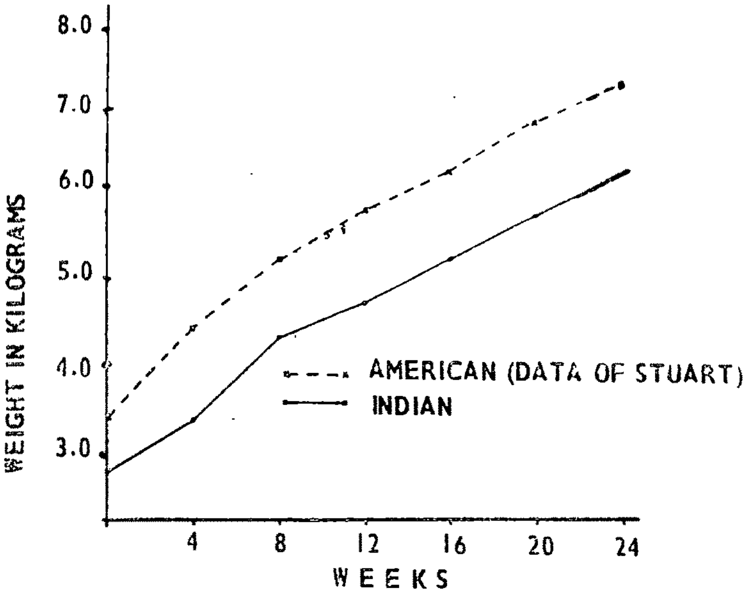
*The figures are the mean with standard error.

Source : Venkatachalam, P. S., Belavady Bhavani and Gopalan, C. 1962. **J Pediatr 61**, 262.

Lactation

It is thus seen that the erstwhile nutritional status of the pregnant women and new borns is unsatisfactory. However, studies on breast feeding practices prevalent in our poor communities have revealed a very heartening and encouraging situation. Breast feeding is universally practised and usually starts around the 3rd day after birth. Mothers do not experience any difficulty in the initiation of lactation and are able to feed the child for long periods sometimes upto 2 to 2½ years. Ninety to ninety-five per cent of the women feed the infant entirely on breast milk for a period of 6 months. However, the quality and nature of supplements given to these children are far from satisfactory. Use of milk from other sources is rare. The growth of the infants is satisfactory till about 5-6 months as shown in Graph 2. The infants are also comparatively healthy and morbidity is low during this period.

Graph 2. Growth of infants.



WEIGHT CURVES OF AMERICAN AND INDIAN INFANTS

The dietary intake of nursing women is shown in Table-VIII. It is seen, that, as in the case of pregnant women, the diet is deficient in all nutrients. Quantitative studies on the yield of milk have demonstrated that they are fairly satisfactory (Gopalan, 1958). The yield of milk, body weights of mother and baby are shown in Graphs 3 and 4. From the second Graph, it will be observed that even while the mother was nursing her infant, she conceived a second time but did not stop feeding the baby. Soon after the second child was born, she took to feeding the new born. It would appear that women in these communities, pass through the stress of pregnancy or lactatation or both continuously during the reproductive period. The abilities of these mothers to secrete such satisfactory amounts of milk in spite of the poor dietary intake has proved to be an enigma. The composition of the milk is given in Tables IX and X. It will be seen that the energy and protein content of the milk are comparable to those of milk from well-nourished mothers. The concentration of vitamins is a direct reflection of the intake.

Table VIII. Nutrient intake of lactating women with the recommended dietary allowances.

Nutrients	Actual intake	Recommended allowances	% Deficit
Calories	1800	2700	33
Protein (g.)	44	65	28
Calcium (mg.)	280	1000	72
Iron (mg.)	20	30	33
Vitamin A (I. U.)	800	4000	80

Source : Gopalan C. and Belavady Bhavani 1961. **Fed Proc 20,** 177.

Table IX. Chemical composition of human milk.

	India[1]	American[2]	British[3]
Protein g%	1.06	1.06	1.16
Lactose g%	7.51	6.8	6.95
Fat g%	3.42	4.54	4.78
Calcium mg%	34.2	34.4	29.9
Phosphorus mg%	11.9	14.1	13.0

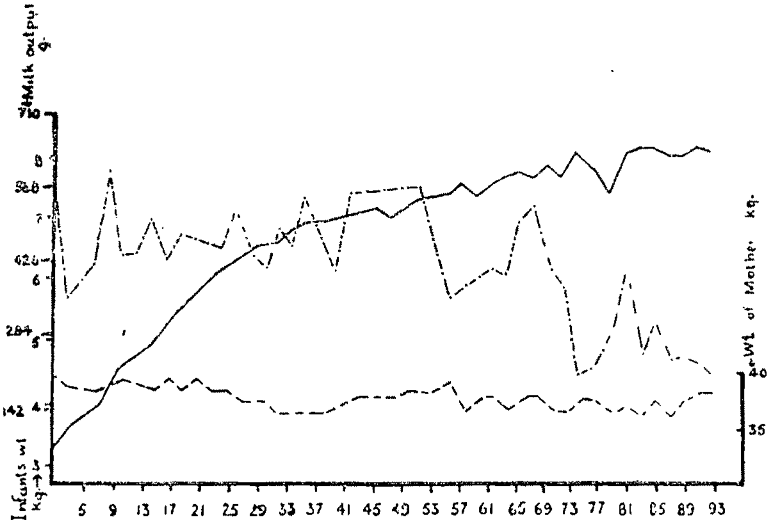
[1] Belavady Bhavani and Gopalan. 1959. **Indian J Med Res 47,** 234.
[2] Macy, I. G. 1949. **Am J Dis Child 78,** 589.
[3] Kon, S. K. and Mawson. E. H. 1950. **M. R. C. Spl. Rep. No.** 269.

Table X. Comparison of vitamin content of milk.

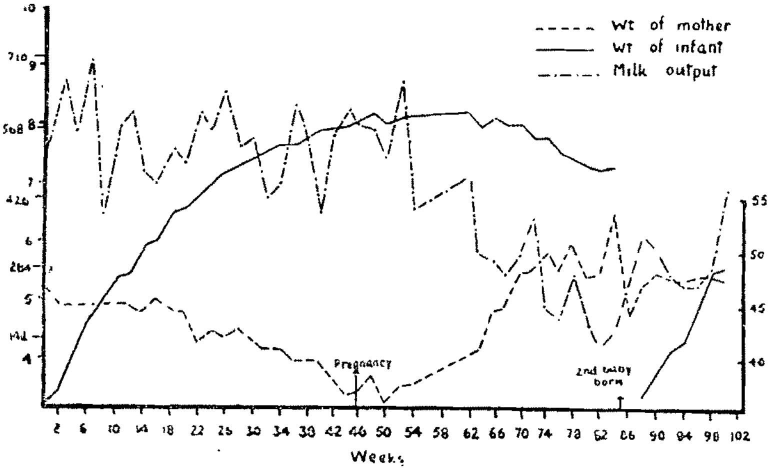
Constituent	Indian	American[2]	British[2]
Vitamin A (μg/100 ml)	23.3[1]	67.0	51.0
Riboflavin (μg/100 ml)	17.2[1]	37.3	25.5
Vitamin C (mg/100 ml)	2.6[1]	5.2	3.2—4.0
Pantothenic acid (μg/100 ml)	230.0	246.0	—
Nicotinic acid (μg/100 ml)	57.0	183.0	—

1, 2 and 3 refer Table IX.

Graph 3. Yield of milk and body weight of mother and infant.



Graph 4. Yield of milk and body weight of mother and infant. Note that the mother continues to feed the child inspite of having conceived.



The height, weight and haemoglobin of nursing mothers are given in Table XI.

Table XI. Height, weight and haemoglobin in nursing mothers of different parties.

	Parity	
	1—3	>3
Weight (Kg.)	41.65 (88)	41.71 (72)
Height (Cm.)	148.11 (74)	148.0 (58)
Haemoglobin (g%)	12.52 (33)	11.47 (23)

Source : Belavady, Bhavani and Gopalan, C. 1959. **Indian J Med Res 47**, 234.

The effects of supplementation with calories, proteins, minerals and vitamins were studied to examine the inter-relationship between dietary intake and the composition of the milk secreted. It was observed that calories and protein supplementation for periods ranging from about 4 weeks to as long as 6 months did not have any significant effect on the yield of milk or on the concentration of protein. The milk secretion in these women initially ranged between 400 and 500 g. per day and it is possible that calories and proteins do not make any impact if the yields are already high. It remains to be seen whether such dietary supplementation would prove effective in instances where secretion of milk may be of a very much lower order. Supplementation with vitamins increased their concentration in milk (Belavady and Gopalan, 1960).

Summing up our observations, the nutritional status of pregnant women is very unsatisfactory. Corrective measures must be taken immediately to mitigate some of the very severe deficiencies. On the other hand, nursing women appear to be fairly healthy. The mechanism of self-correction which follows parturition is not clear. The nutritional stress of milk production is not any less than the stress of pregnancy.

The dietary intake in both these conditions is far from satisfactory. Attention must be paid to improve the diets. The cultural pattern of prolonged breast feeding among women is a great asset and we must make all attempts to preserve and foster it. The problem of malnutrition among infants is likely to be aggrevated with the introduction of artificial feeding. Infection and infestation are bound to increase. Further, breast feeding has been found to be associated with longer birth interval and will indirectly contribute to our efforts at limiting family size.

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The Problem of Anaemias in Pregnancy

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Introduction

Anaemia is the most common medical disorder seen during pregnancy. It constitutes an important cause of maternal morbidity and mortality in our country. Maternal mortality from anaemia is very high in India and is considered as the second cause of death among pregnant women. The incidence of maternal mortality ranges from 10 per cent to 20 per cent in different part of our country. The high incidence of anaemia in pregnant women has been recognised. The deficiency of iron and or folic acid as the cause of anaemia has been emphasised by many. The incidence and type of anaemia shows considerable variation depending upon the socio-economic and nutritional status of the people. The great majority of patients are poor economically and nutritionally.

Incidence

Nearly, 92 per cent of cases are anaemic when 10 g. per cent of Hb is considered permissible as low normal level of Hb in pregnant women. When Hb per cent falls to or below 6 g. per cent, it is considered as the critical level of Hb. Iron deficiency alone accounts for 73 per cent of the cases, the single most common cause of anaemia during pregnancy. In one third of cases in pregnancy, the anaemia is of dimorphic type. Between 30 and 66 per cent of women show incidence of megaloblastic change in bone marrow due to folic acid deficiency. Vitamin B_{12} deficiency is rare during pregnancy.

Etiology

The etiology of iron deficiency anaemia is complex. The inadequate diet, unsatisfactory methods of preparation of food, faulty social habits, lack of proper hygenic measures, religious dogmas, associated infections and infestations are the main factors which continue to perpetuate anaemia The iron content of average diet is 30 to 50 mg. per day. This iron in a vegetarian diet is equivalent to 1.5 to 2.5 mg. of available iron to the body and is presumed to be enough for the maintenance of iron stores at a normal level. At the same time, the high content of phytic acid forms insoluble iron phytates and phosphates and thus causing inadequate iron stores to meet the foetal demands for iron in the average Indian women. Pregnancy imposes a substantial burden on the female. During pregnancy the extra iron required is in the region of 1400 mgs. The total deficit by the end of pregnancy is 775 to 1000 mgs. A woman needs therefore, to absorb 2.8 to 3.6 mgs. daily to provide for the needs of her pregnancy. A pregnant woman thus needs more iron than she can get from a normal diet.

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The commonest cause of anaemia found in pregnancy is iron deficiency. This is due to extra foetal demand during pregnancy. The amount of iron that a woman saves due to amenorrhoea of pregnancy is insufficient to counterbalance the drain of iron into the growing foetus. This obviously aggravates maternal deficiency. The storage of iron may be seriously depleted at the onset of pregnancy. The intake of iron may be inadequate or absorption from the intestine may be at fault or the erythropoiesis may be depressed. Rapidly occurring pregnancies without an interval for recovery, cause a woman to become anaemic. The loss of blood from peptic ulceration, haemorroids or tropical parasites, leads to depletion of iron stores. Early morning sickness or a diet poor in iron content may further reduce the intake of iron. It is possible that any infection in the body is likely to depress the erythropoiesis.

As in the case of iron, several such factors keep the dietary supply of other haemopoietic principles, namely folic acid and or B_{12}, very marginal. Like iron, the foetal demands of pregnancy lead to shortage of these haemopoietic factors also. The turn-over rate of folate in the body being very quick, it suffers an immediate serious setback, whereas the turn-over rate of B_{12} is so slow that 40 weeks of pregnancy is a short period to develop complete exhaustion.

Symptoms : The patient feels tired, listless, giddy and complains of headache. Palpitation may occur and there can be oedema over ankles. Anorexia and indigestion are common symptoms. She feels general weakness. Soreness of tongue, vomiting and diarrhoea are more common due to folic acid deficiency.

Diagnosis : From every point of view it is desirable that the Hb should be estimated on at least three occasions during pregnancy. First estimation is in early pregnancy, the second at 28 weeks and the third at 36 weeks. It must be emphasised that it is not possible to judge with accuracy whether a patient is anaemic or not from inspection of the skin and mucus membrane. Hb per cent, RBC, MCHC and MCV are reduced and the stained film shows anisocytosis, microcytes and poor staining of RBC in iron deficiency anaemia.

In folic acid deficiency, most patients have progressive anaemia in the latter half of pregnancy which has failed to respond to treatment with iron and Hb is very low. Megaloblasts are found in the peripheral blood. Bone marrow shows megaloblasts and giant metamyelocytes. Achlorhydria is found in about one third of patients.

Complications : When iron deficiency anaemia is severe, premature delivery is more frequent and foetal anoxia may cause intrauterine death of the foetus. Anaemia is a major cause of maternal and foetal mortality. There is increased incidence of primary uterine inertia and prolonged labour. There is increased liability to venous thrombosis, diminished resistance to bacterial infection and failure of lactation in puerperium. Folic acid deficiency is likely to produce abortion, foetal malformations and accidental haemorrhage, in addition to above complications.

Treatment

Prophylactic : Improvement of socio-economic conditions and dietary standard is no doubt essential for the control of anaemias. It is time for the medical men to suggest ways and means which should be able to offer immediate benefits from out of the available national resources. Population control by planned parenthood is no doubt an essential pre-requisite. Its utility and importance can't be overemphasized. It is necessary to take direct steps for the immediate correction of existing deficiencies. An alternative course to provision of adequate diet with sufficient amount of all the essential nutrients is to provide a fortified diet or dietary supplements. It would be ideal if the flour in India could be fortified by the addition of iron, folic acid and Vit B_{12}, which would not effect the taste and digestability of flour. In order of priority, the claim of iron is the foremost and next in the list is folic acid.

A reference to the method of cooking in India needs mention. The practice of employing iron utensils for cooking and utilization of water, in which rice and vegetable are cooked, will help in adding some iron to the food and prevent loss of iron and nutrients. These two procedures entail no additional expenditure and can be universally adopted. There can be no doubt that iron deficiency anaemia of pregnancy should be prevented rather than cured. It seems good reason for giving all women iron by mouth during pregnancy and lactation. It should start after the 20th week to avoid increasing the early vomiting of pregnancy. Ferrous sulphate, 9 g. orally can be given in three divided doses after meals. All pregnant women should be encouraged to eat plenty of green vegetables and meat or pulses.

Curative : When anaemia has developed, treatment can be carried out by mouth provided she is early in pregnancy and anaemia is mild or moderate. If intolerant to iron by mouth, it can be given parenterally. Women who have severe anaemia and near term are best treated by total dose of iron dextran complex by intra-venous route. The total dose can be calculated and an extra 500 mg. of iron dextran is added for the need of the foetus. This method has the advantage of single dose therapy, short stay in hospital and it helps to replenish the depleted stores.

All pregnant women under 35 years of age should get 3 mg. of folic acid daily throughout pregnancy, or 10 mg. daily from 28th week. Therapeutic dose for folic acid in megaloblastic type of anaemia is 10 mg. thrice daily by mouth. If labour is imminent and anaemia is severe, probably the most effective treatment is blood transfusion. Exchange transfusion with packed cells is also indicated in selected cases.

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The Problems of Female Children

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Children constitute the most vulnerable part of any society. This is particularly so in the developing countries. Even among children, adverse socio-economic and cultural factors seems to impinge more on the health of the female compared to the male children (Wyon and Gordon, 1971).

Some of the disadvantages of the female sex are evident even at birth. Thus all over the world, larger number of male babies are born compared with the female babies (U. S. Department of Health, Education and Welfare 1967) and the difference is probably the highest in India (UNICEF, 1974 ; Table I). Average weight and other anthropometric measurements at birth are lesser in females, than the males (Ghosh and Berry, 1963). A larger proportion of female children, therefore, are low birth weight i.e. below 2000 g. However, the incidence of congenital malformation is lesser in females (Safdarjang Hospital, 1972 Table II).

Table I. Sex ratio, males per 1000 females at birth.

India	1116
England	1066
Europe	1060
U. S. A.	1047

Source : U. S. Department of Health, Education & Welfare, Vital & Health Statistics, Series 3, No. 6, pp. 56.

Table II. Characterstics at birth.

Sex	Average Birth Weight (gms.)	L. B. W. (%)	Congenital Malformation %
Male	2774	6.5	4.0
Female	2704	8.5	2.7

Source : (i) Ghosh, S and Berry, S. **Criteria of prematurity for north Indian babies. Indian J Child Health,** 1963.

(ii) Records of Safdarjang Hospital.

The females weigh less than the males at almost all ages, except between 11-13 years which is due to the earlier prepubertal spurt of growth in females. In our country the difference between males and females are exaggerated between 1-3 years (Narangwal Health Research Centre 1972). This is probably due to a higher incidence of malnutrition among females (Narangwal Health Research Centre 1972), which in turn is due to deeprooted social and cultural beliefs.

An impression of higher male morbidity is created if the statistics of the out-patient department and indoor admissions to the pediatrics wards are seen. Thus at the Safdarjung Hospital, both at the out-patients and in the admission to the pediatric wards male out-number females by almost 3 : 2. The ratio, however, is reversed when we look at the figures of attendance at the Nutrition Clinic of Safdarjang Hospital where children attending the out-patients and found to weigh below 60 per cent of the expected weight (III degree malnutrition) are referred. There are 54 per cent females and 46 per cent males (Table III). This substantiates the view (Narangwal Health Research Centre 1972) that malnutrition is higher among female children as compared to the male children. This could be the reflection of inadequate care and an inherent prejudice of parents towards a female child.

Table III.

	Female	Male
Hospital admissions	36%	64%
O. P. D. attendance	39%	61%
Nutrition Clinic attendance	54%	46%

Source : Records of Safdarjang Hospital.

The early age of marriage and the long reproductive period with repeated pregnancies would have an adverse influence on maternal mortality as well as the infant and early childhood mortality (Wyon and Gordon, 1971). It is well known that the birth weight goes on decreasing with successive pregnancies and the prevalence of malnutrition is far higher after the 4th birth order. Since the birth weight of the female children is lower and the incidence of malnutrition among them is higher as compared to the males, the adverse effect of repeated pregnancies will be felt far more in the female children. In our country, 13 per cent of the girls between 10-14 years and 56 per cent of the girls between 15-19 years are married (UNICEF 1974). Pregnancy in a very young mother is more risky, leading to a high maternal and perinatal mortality rates.

The impact of social and cultural factors on the health status of females will be evident if one looks at the figures available from Kerala (Govt. of Kerala, 1974). Keralites have the highest functional literacy in India (UNICEF, 1974). The differences are even more marked when one sees the standard of female literacy in Kerala and compare with the all India figures (CBHI, 1973, Table IV). This is probably responsible for a higher mean age at marriage among the girls in Kerala and has resulted in a sharper decline in birth rate in Kerala, compared to All India average (Govt. of Kerala, 1974 ; Table V). Also the life expectancy in Kerala is higher for females in contrast to the all India pattern (C.B.H.I. 1973 ; Table VI).

Table IV. Functional literacy India (in percentage).

	Male	Female
Kerala	80.7	89.2
All India	46.6	41.5

Source : Government of Kerala, **Economic Review,** 1974.

Table V. Birth rates in Kerala and India (Per 1000 Population).

Period	Kerala	India
1931-40	40.0	45.2
1941-50	39.8	39.9
1951-60	38.9	41.7
1968 (Rural)	33.2	39.0
1970 (Rural)	31.9	38.8
1972 (Rural)	31.5	38.4

Source : Government of Kerala, **Economic Review,** 1974 p. 35. Registrar General, Sample Registration Bulletin, Vol. VIII, No. 1, April 1974.

Table VI. Life expectancy.

	Male	Female
Kerala	60.6	61.2
India	48.2	46.2

Source : Government of Kerala, **Economic Review,** 1974.

The studies in mortality reveal interesting pattern. Male mortality is high throughout life in all developed parts of the world (U. S. Deptt. of Health Education and Welfare 1967) but in India the female mortality is higher throughout life except the first week (UNICEF, 1974, Vital Statistics Division, 1971; Tables VII and VIII) resulting in a low expectancy of life in the females as compared to the males. This is in contrast to the observations from the developed parts of the world, where the expectancy of life is higher in the females.

Table VII. Estimated mortality.

Sex	Up to 1 year	1—4 years	5—14 years
Male	132	7.6	1.33
Female	148	8.1	1.32

Source : Statistical profile of children and youth in India, UNICEF, New Delhi, 1974. Rates calculated from total deaths and mid year population in various age groups.

Table VIII. Sex-wise mortality.

Sex	Perinatal	Neonatal		Postneonatal
		Early	Late	
Male	70	44	30	58
Female	60	41	35	72

Source : (Same as table VII).

The sex ratio has been progressively declining in India from 972 females per 1000 males in 1901 to 930 females per 1000 males in 1971 (Ministry of I. & B. 1975) The reasons for this are not very clear but inherent cultural patterns and prejudice against the female children resulting in a high death rate among them seem to be the contributing factors. A pattern similar to the developed countries is seen in Kerala with a higher number of females (1016) per 1000 males (UNICEF, 1974).

Table IX. Sex ratio 1901-1971.

Year	Females/1000 males
1901	972
1911	964
1921	955
1931	950
1941	946
1951	945
1961	941
1971	930

Source : India, 1975 P. 9.

The preference for sons leads to a high birth rate because of high infant and pre-school mortality (Wyon and Gordon, 1971). There are deep rooted cultural and social beliefs regarding this, which have to be taken into account in planning of any family planning campaign. The family planning publicity material always showing one girl and one boy is in a way perpetuating this belief.

The highlights of the problem then seem to be a higher death rate and a higher incidence of malnutrition among the female children. To deal with these, a sustained education of the population, better socio-economic and cultural climate and a higher education level especially of the females will be required. A co-ordinated approach by both Government, and voluntary agencies in the sphere of social work. education, women's welfare, health care etc. is essential to emancipate the Indian women from these problems.

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Women in Industry

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In Ahmedabad women, in association with their men folk, are employed by occupation in pulling loads to the extent of 1000 kg. using handcart, and they usually walk a distance of 8 to 10 km. a day. It is a common sight in Ahmedabad and, probably, the only place in the world.

The handle of the bar of the cart constantly touching the lower part of the abdomen of women cartpullers while pulling the cart. This may have some effects in their menstrual circle or may cause abortion in the early stages of pregnancy.

A study was initiated by the N. I. O H. to find out the physiological cost of pulling loaded handcart with loads of 300 kg. 500 kg. and 1000 kg. including the weight of the empty cart. The parameters taken were pulse and energy cost of pulling. The subjects were divided into three different age groups of 20-29, 30-39, and 40 and above. It was found that the physiological cost of pulling the loads increased with increase of loads. After carrying out a number of studies on the conventional cart, the cart was redesigned in such a way that there is no need for lifting the cart for pulling and there is a margin of safety between the handle of the bar and the body while pushing, by way of increasing the length of the cart. There is also provision for keeping the tiffin and a cradle to keep their babies. There was no provision for brake in the conventional cart, and the cartpullers use their legs for braking purpose. Provision for braking has been made in the redesigned cart. The same subjects were used to study the physiological cost of pushing the redesigned cart with varied loads of 350 kg. 500 kg. 750 kg. and 1000 kg. including the weight of the empty cart. It is very gratifying to mention that there is a reduction of 12-16 per cent in the physiological cost for pushing loads with the redesigned cart. The pulse rate was reduced to 170 beats/min. in case of women pullers while pushing 1000 kg. weight to 130 beats/min. at an average with the redesigned cart. This redesigned cart will be of help to these cartpullers in reducing the physiological cost while pushing varied loads.

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Psychological and Social Problems of Women

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Indian women have won their political, economic and social rights like their counterparts in other countries. These rights have been translated into realities without adequate preparation of the incumbents who draw their rights from these changes. The emancipation of women has released powerful social forces which, in turn, have affected women psychologically. The International Womens' Year has served in highlighting not only the achievements of women, but also the drawbacks and disadvantages of this emancipation. The forces are already geared to action ; we therefore have to prepare those who are to be affected, and assist those already in the race, to overcome these problems.

On the threshold of womanhood, freed from apron strings and school discipline, the young lady just after her school career, has to plan her future. Freedom of choice of occupation, equal rights, availability of responsible, high prestige and risk ridden jobs, and equally secure but less exciting ones, leave the individual in quite a dilemma, as to where to go next. Decision making which was her guardians privilege until recently, is now in her hands. To those who would like to enter womanhood with the assistance of a partner the marriage market offers various choices. Here again, those in authority are reserved in their opinions and the modern girl is left to choose for herself. Wise parents may succeed in some human engineering : those less endowed may wait and pray for wisdom to dawn on their daughters. Educational opportunities all over the world facilitated by availability of scholarships, invitations, variety of subjects, and areas of specialisation, magnetise those with a flair for academic achievement. Social and financial conditions of the home, religious and cultural attitudes and norms of the family, the effect of school education, and individual aptitude and physical and mental capacity are the various forces that play on the individual, in the final decision. This may be to continue studies, start a career, or to marry.

Women who choose an academic career may do so only as a stepping stone to a married life, as a preparation for greater responsibilities. Others make a more serious issue of their early college years, which, for them, is a preparation for higher academic achievement. This period, in either case, is fraught with indecision, conflicts, adjustment problems, and, in the more forward section, with drug habits, sexual irregularities, promiscuity and delinquent behaviour. These disturbances are etiologically located in faulty homes and parents, and inadequate teacher-student ratio, resulting in deficient understanding of, and attention to the students.

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A career woman who has chosen an all-absorbing area of work will find immense satisfaction if she devotes herself to it entirely. But this contentment will last only as long as the job satisfaction lasts. She may feel socially isolated and deprived when opportunities to bury herself in her work are denied for some reason or other. If she does not cultivate hobbies and interests to sustain herself outside the framework of her job, she will suffer at a later date when physical and psychological deficits render her unsuitable for her chosen career.

The working woman who chooses to marry will have to organise her job requirements and domestic duties in such a manner that they do not interfere with each other. Adjustment problems, inadequate communication with husband and children, role changes with reference to earning partner, likelihood of the female domineering, too much confidence and self-reliance, make it difficult for women to play the twin roles successfully. While the charm of extra emoluments may secure male appreciation of a working partner, the experience of incompatability and negligence of children may change his attitude. The working mother exposes herself to considerable strain, and needs assistance from the school and community to maintain her stability. The nuclear family with reduced social support is not very conducive to rendering assistance in this area.

To live a life and secure the maximum joys of all that it offers, one needs to streamline one's emotional life, and this can be achieved only by an intellectual preparation at every stage of existence for the next arena of competition and frustration. Defects in one area can always be compensated for in others, but wisdom and opportunity may come too late to make this a reality.

Choice of a partner is a crucial issue. Our grand fathers matched families and heritage : our computers will match temperaments. Between the two we have all that is left to cultural restrictions, religious taboos, social incompatibilities, and financial considerations. Torn between these two extremes, both generations are trying to adjust to each other, and for both, this subject becomes a problem. Immature infatuations have to enter into the differential diagnosis of arrangements for marriage, as much as a tempting dowry or the desire to maintain a financial wholesomeness, as seen in alliances which aim at security of the family income, rather than consider the inadvisability of consanguinity. In modern times, marriage is a gamble with life, and women have to be prepared and equipped to take a victory and a defeat with equal grace.

The popularisation of family planning has its own serious repercussions on women. Those less educated and clinging to old ideals find it difficult to accept. When basic doubts are cleared, the idea of seeking sex for mere pleasure rather than for procreation creates guilt and disgust. Therapeutic abortion without sterilisation may result in similar complications. When sterilisation is associated with abortion, a sense of uselessness prevades the woman. She feels she has lost her feminine qualities, and will be neglected by her husband. It has been found, in abortion clinics, that women who voluntarily come forward for therapeutic abortion, refuse sterilisation if compelled. From her partner's view-point she is now free from fear of pregnancy, and may therefore seek sexual pleasure elsewhere. Mutual distrust results in considerable disturbance in marital and domestic relationship. Permissiveness, promiscuity and prostitution can be expected in a population where values have changed considerably, and religion, faith, respect for elders, and confidence in parents have crumbled to irreparable ruin.

If youth is full of indecision and immaturity, and the adult ridden with responsibility and adjustment to family and work, the ripe years of experience insulate the middle aged but leave them with deficits, disease and degenerations which need considerable coping. Having lost her youth, the woman feels she has receded to the back rows. The **joie de vivre** has left her and she looks forward with dread. Physiologically she suffers more than men at this period. Retirement, social isolation, financial insecurity and emotional vacuum call for special coping mechanisms which have to be cultivated and developed earlier in life. In the joint family she slipped aside and enjoyed the position offered as mother-in-law : she might have been held in awe, respected, revered, idolised, idealised or hated ; but she ruled. The nuclear family sees the children leaving one by one to find their own homes with scant consideration of their responsibilities to the older generation and parents. Leisure hangs heavily on her resulting in boredom, frustration, and sickness.

No home now, if adequately modern, accepts voluntarily, the care of the aged. Economically they are a burden, socially they are embarrassing, and their poor physical state may demand more attention than can be afforded. So, for the older woman, depression follows when resignation is difficult.

By virtue of her sex, woman is subjected to considerable psychological and social stress and strain. Equal rights and job opportunities will not alleviate this. The recognition of the woman as equally important as man will highlight her difficulties which will seek platforms for settlement by those in authority—leaders of opinion, politicians and policy makers. Assistance to women in the youthful years, with adequate guidance and counselling at the college level for decisions regarding their future, for recognition of their feelings, and for the development of a healthy personality, will go a long way to save them from future trouble. The counselling must be set in the natural environment of the college and must be intricately woven into the fabric of education and training. Vocational counselling centres for advice on job opportunities and feasibilities will orient the young woman to a planned and organised future. Marriage counselling, before and after marriage, will be necessary for her in the near future. Better relationship between parents and teachers will help to solve problems related to her children. The cultivation of hobbies, and healthy leisure activities, can take women peacefully through middle age to old age. Homes for the aged are becoming popular now, and for the older women, a home away from home is an inevitable consequence of the increase in the nuclear family.

The advantages of every progress is beset, or equally balanced, by disadvantages. Psychological and social problems of women given equal place with men call for an extra effort on the part of women to meet this challenge, and on the state to help their women to live up to the liberty they have been given.

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Rapporteur's Report II

Report of Scientific Session II—Nutrition and Health Aspects

Chairman : Dr. (Miss) S. Padmavati

Rapporteur : Dr. Satya Gupta

The IInd Scientific Session was chaired by Dr. (Miss) S. Padmavati. There were four speakers. Dr. Sharda Menon who was to have spoken on Psychological and Social Problems of women could not attend the session.

First paper was by Dr. Bhavani Belavady on 'Nutrition in Pregnancy and Lactation'. She highlighted the nutritional deficiency in pregnant and lactating women and substantiated these facts by certain slides showing that the daily intake of majority of women was roughly 57 per cent in terms of calories, 37 per cent in terms of proteins and was also deficient in iron, calcium and vitamin A. Nutrition became worse as the parity of the mothers increased. She also showed that a normal healthy pregnant woman gains 10-12 kg. of weight during her pregnancy as compared to 6 kg. by woman belonging to low socio status. The birth weight of the infants born to mothers from low socio groups was also significantly low. Similarly the incidence of premature pregnancy and low birth weights were high in these groups. This was again documented by their studies with women who had supplementation of their diet with vitamins, proteins and calories, even if the supplementation was made during the last 4-5 weeks of gestation. Similar supplementation with vitamin A brought significant increase in the vitamin A concentration in cord blood. Protein beyond 60 g. were not effective in increasing the weight of the new born but increase in calories had a direct relation to the weight of the infant. She stressed on breast feeding. According to her, 90-95 per cent of women breast fed their infants for a period of 6 months without any supplementation. Morbidity in these infants is low. It is interesting to note that despite the fact that nutrition of these nursing women is deficient in all nutrients, quantitative studies on the yield of milk was good enough and mothers are not adversely affected. Milk was not deficient qualitatively as well in majority except for vitamins which were low compared to western women, since it is a direct reflection of the intake. The impact of supplementation for periods ranging from 4 weeks to 6 months in terms of calories and proteins did not have any significant effect either on the yield of milk or on the concentration of protein. Initially milk secretion was 400-500g. per day. She summed up by saying that the nutritional status of pregnant women in this country is very unsatisfactory. She recommended collective measures for mitigating some of these severe deficiencies. On the other hand lactating women appear to be fairly healthy. Despite the fact that nutritional stress of milk production is not any less than the stress of pregnancy She recommended breast feeding because of the increased incidence of infection, infestations and associated malnutrition with the introduction of artificial feeding. She also made a mention of the association of breast feeding with increased interval between two births.

Next paper was by Dr. S. N. Mukherjee on Anaemia in pregnancy. He stressed the point that anaemia in pregnant women is one of the most common medical disorders. Maternal mortality from anaemia is very high and is considered as the second cause of death among pregnant women. Nearly 92 per cent cases are anaemic when 10 g. of haemoglobin is considered as low normal for these women. Iron deficiency alone accounted for 73 per cent in a series. One/3rd are dimorphic and 30-66 per cent showed megaloblastic change. Vitamin B 12 deficiency was considered rare by him. He stressed the point that anaemia is a problem common to us the developing countries and has no importance in the western world. Over the years when infections have lessened and other improvements have been made the incidence of anaemia remains roughly the same. Pattern is similar all over the country. Iron deficient anaemia is the commonest amounting to 60-70 per cent followed by folic acid. B12 deficiency being the least common. The etiological factors were stressed varying from deficient diet, social customs and parastic infestations. During pregnancy the extra iron required is in the region of 1400 mg. The total deficit by the end of pregnancy is 775 to 1000 mg. Therefore, it was pointed out that a pregnant woman needed large quantity of iron which she cannot get from a normal diet. Rapidly occurring pregnancies without an interval for recovering may further aggravate anaemia in women. He recommended that haemoglobin should be estimated atleast 3 times during the course of pregnancy. First estimation should be done as early as possible, second at 28 weeks and third at 36 weeks. Since anaemia has wide spread implications ranging from fetal anoxia which may end up in intrauterine death of the fetus to premature delivery, besides uterine inertia, prolonged labour, increasing liability to venous thrombiosis, fetal malformations, accidental haemorrhage and small weight babies. It was suggested that all pregnant women should be given iron and folic acid supplementation. He also commented on the method of cooking in India employing iron utensils which impart some additional iron to the food. According to him all pregnant women under 35 years of age should get 3 mg. of folic acid throughout pregnancy besides the additional iron in women who were deficient in iron. He suggested total dose of iron, dexton complex with 500 mg. of added iron for the infant may be done to save repeated therapy, he recommended prophylactic fortification of flour by iron, folic acid and B_{12}.

Next paper was by Dr. Shanti Ghosh on the problems of female children. In this paper she highlighted the impact of adverse socio-economic and cultural factors right from birth in as much as the average weight and other anthropometric measurements are lesser in females as compared to males. The males have an apparent increase in the mortality and morbidity only in the 1st week of life to be followed by higher mortality rate in females, right from late neonatal period till about 4-5 years of age. She showed her own hospital statistics from which it was clear that more males attend O.P.D. but the incidence of malnutrition is much higher in females. Further 13 per cent of female under the age of 14 got married in the country which added to ill health and stresses during a period of pregnancy and lactation. For the impact of social and cultural factors she mentioned the figures from Kerala where the functional literacy is highest, both for females and males with the result that there is a higher mean marriage age in Kerala which probably results in sharp decline in birth rates.

Next paper was by Dr. Chatterjee on the problems of women in industry. This was an interesting paper in which he showed the falling incidence of women in industry, except for agriculture labour. He showed a study on the female cart pullers in Ahmedabad and the improved version of the cart on which these females and males showed better adjusments physiologically.

Next paper should have been by Dr. Sharda Menon on the Psychological and Social problems of women. Dr. Sharda Menon could not attend the session and hence the paper was taken as read. In this paper she highlighted the psychological and social problems starting from a young lady who has just finished her school career. Her dilemma in terms of occupation or wishing to get married are projected. These are inadvertently affected by social and financial conditions of the home, religious and cultural attitudes, norms of the family and effect of school education etc. She mentioned the problems of career women who choose an all absorbing area of work. Her problems in regard to social isolation and deprivations together with little time for the development of hobbies and interest may effect at a later date when physical and psychological deficits render her unsuitable for her chosen career. The problems of a working married woman in terms of adjustment, inadequate communication with husband and children make it difficult for her to play the twin role successfully. The working mother exposes herself to considerable strain. Emotional problems associated with sterilisation were also mentioned. She also made a passing reference to the problem of women from nuclear families when children leave to find their own houses, leisure hangs on heavily on the woman of the famity resulting in boredom, frustration and sickness She further stressed on the importance of assistance to women in their youthful year with adequate guidance and counselling so as to help them develop healthy leisure activities which will go a long way in taking women through middle age to old age, thus helping them to live up well and independently.

Scientific Session III

Family Planning

Ann Indian Acad Med Sci, 12,4, Oct—Dec 1976

Current Status of the National Family Planning Programme—its Needs, Objectives and Effects

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Needs

Population growth and Family Planning : In recent years the world population has been increasing by about 65 million annually of which the developing countries account for 55 million. The current yearly growth rate is 1.9 per cent. The developing countries accounting for 2.37 per cent as against 0.8 per cent in the developed nations. Steep and rapid reduction in death rate without a commensurate fall in births is largely responsible for this imbalance on our planet. The impact of this enormous increase in population can be visualised in the social and economic upheavels which the developing countries are passing through. In the Western countries rapid population growth and structural changes in socio-economic development, increased investments of man-power and phenomenal technological advances went hand in hand together leading to reduced fertility and a fresh balance. In order to influence high population growth rate combined with a low socio-economic development special measures have had to be instituted in India. Due to high fertility and reduced mortality about 42 per cent of the population is below 15 years of age. The dependency rate is thus 80 per cent compared to 57 per cent in the more advanced nations. India is the second largest country in the world with an estimated population of 600 million in 1975 with an annual growth rate of 2.2 per cent. It accounts for 14 per cent of the world population with only 2 per cent of the land area. This unprecedented increase in human beings has largely nullified the fruits of economic advancement. Food production doubled in 1970-71 compared to 1951 but the per capita grain improved only from 395 g. in 1951 to 467 g. in 1971. Similarly, the national income increased by 108 per cent during 1951-71 but the per capita increase was only 38 per cent. The estimated vital statistics of India based on Sample Registration data indicate an increasing growth rate which was maximum during 1961-71. India's population which was a little over 250 million during 1911 to 1921 exceeded 360 million by 1951, was approximately 440 million by 1961 and 548 million by 1972. It is at present around 600 million. If fertility continues unabated this figure would be doubled by the turn of the century.

Objectives

The national programme of family planning was started in 1952 in the first Five-Year Plan by the Government of India. This was the first nationally sponsored programme. Initially this was confined to providing family planning advice to the people coming in the government hospitals and rural medical centres. A more vigorous action-cum-research programme was undertaken in the second Plan. The clinic approach of the first two plans was replaced by extension education carrying the message and services to the people at their door-steps covering every nook and corner of the country. Measures were also instituted to involve voluntary organisations and local leaders. By offering a number of different methods of family planning a cafeteria system was developed. During the inter-plan period 1966-69 the strategy was given a more concrete and definite shape. Since 1966-67 the programme has become target-oriented with the objective of reducing the annual birth rate. On April 1966 a separate Department of Family Planning was constituted in the Ministry of Health to give technical and administrative guidance to the programme and laying down broad policies. The organisational set-up in each State constitutes a State Family Planning Council, a State Family Planning Bureau under the Directorate of Health Services. Each district has a district F. P. Bureau with its complement of Urban Family Welfare Planning Centres and the Rural Family Planning Welfare Centres each servicing a population of 80,000 to 100,000 as an integral part of the Primary Health Centre. High priority continued to be assigned to the programme and an outlay of 330 crores was provided in the Fourth Plan against 26.98 crores in the third Plan. Inspite of the grave economic crisis with the unprecedented price increase of oil, fertilizers and food imports the allocation of the Fifth Plan is 516 crores an increase of 56 per cent over and above the Fourth Plan budget. The objective of laying down targets is to bring down the birth rate to 30 per thousand at the end of the Fifth Plan and 25 at the end of the Sixth Plan. To achieve our operational goal of the Fifth Five-Year Plan about 40 million out of the 110 million fertile couples would have to be covered by some family planning method. Currently only about 17 per cent of women in the reproductive age are protected from the risk of child birth. The stupendous task of fulfilling our targets is by linking health services with family planning thus providing comprehensive health care. The basic strategy is to train special multipurpose workers in the 5416 Primary Health Centres, 33048 sub-centre and 1919 urban family planning centres. One of the reasons for the slow progress of fertility control in our country is scant attention paid to rural health problems. With the upgrading of 25 per cent of the Primary Health Centres under the minimum needs programme health services in the rural areas should receive a big boost. In order to alleviate poverty 3803 crores of rupees have been set aside not only to provide maternal and child health, immunization, nutrition and elementary curative services but also to step up electricity, filtered water, roads, schools and house sites wherever necessary. In this manner the Govt. hopes to launch a systematic attack on rural backwardness and poverty. In short family planning far from being a Government programme should become a mass movement, the demand for services generating amongst the people themselves. Economic compulsions often motivate people to adopt a small family norm but if a large section of the population is at the subsistence level these fail and every additional pair of hands is considered a means of economic advancement. Community involvement which has been relatively negative previously is being vigorously activised by involving village Panchayats, labour and industrial organisations, cooperatives and voluntary bodies like the Family Planning Association of India, Indian Christian Association for Family Planning and many others. A system of incentives and disincentives is being processed.

Effects

Performance : By March 1975, 16.2 million sterilisations have been performed of which 12.1 million were men and 4.1 million women. 5.4 million IUD insertions and 2.4 million users of conventional contraceptives have also been enlisted. It is estimated that about 22 million births have been averted by July, 1975. Consequently the national birth rate should have dropped to 35 compared to 36.6 per 1,000 for 1972 by the Sample Registration data. The performance in the States has been uneven, Maharashtra, Punjab, Haryana, Kerala, Tamil Nadu, Gujarat, Andhra Pradesh and Orissa being about the All-India average of 16.2 per cent. The State of Assam which had tended to lag behind has done exceedingly well in 1975 and if the present tempo is maintained it should soon be competing with the more forward States. In order to correct the imbalance in performance in the different States the targets instead of being allotted on an ad-hoc basis have been calculated on various basic factors like growth rate, density of population, extent of urbanisation, female literacy, level of previous performance and available resources with the demographic objective of reducing the birth rate to 30 per thousand at the end of the Fifth Plan.

Mass Communication : Communication for family planning will be gradually integrated with communication activities under the different developmental programmes so that it becomes a component of the total developmental programme An inter-departmental, multi-disciplinary, multi-professional high powered Communications Board with the Union Minister of Health and Family Planning as Chairman and the Minister of Information and Broadcasting as Vice-Chairman has been set up to guide the implementation of this integrated communication strategy. In order to improve the performance and ensure stability of service, certain posts have been made permanent. The number of regional directors has been raised to 16 to effectively coordinate the work of family planning in the States. The training programme under the Family Planning Programme and the multipurpose workers scheme is continuing and about 3000 workers had been trained until June, 1975.

Special Programme : All-India Hospital Post-Partum Programme was initially sanctioned in 59 medical institutions in 1969-70. Encouraging results obtained in its implementation saw its extension to 256 hospitals by 1975-76. The main aim of this service is to maximise the extent of effective contraception amongst the target population besides focussing attention on other patients attending the hospital and the general community surrounding it. To achieve these objectives the family planning services have been strengthened by provision of additional inputs in the form of staff and equipment including vehicles, buildings for operation theatre and sterilisation ward immunisation, and antianaemic therapy. From January, 1970 to June 1975 2.34 million cases were serviced and of these 0.99 million accepted some method of fertility control. In the quarter ending June 75 the programme improved further total acceptors increasing from 34.3 to 39.3 per cent of all the abortion and delivery cases. Abortion rose from 14.9 per cent of the total cases to 24.3 per cent. Though tubectomy accounts for 50-70 per cent of the acceptors, contraception by other methods is only 25.35 per cent. This is a poor figure and needs to be urgently improved. The programme also has an MCH and immunisation component.

Medical Termination of Pregnancy : The M. T. P. Act came into force on 1st April, 1972. This health measure was mainly passed to eradicate the large number of criminal and clandestine abortions which pose such an enormous health hazard to the pregnant women. Most women however undergoing medical termination of pregnancy are wedded to a small family norm and will accept some method for controlling their fertility. Uptil July 1975 a total of 211766 abortions had been reported from different centres. One thousand three hundred and fifty-two institutions have been recognised and 2776 doctors approved. Medical termination of pregnancy rules have been greatly simplified removing a major handicap in the performance of the important health measure.

Oral Pill Programme : In November 1974 this programme was extended to all urban family planning centres including local bodies, voluntary organisations and to those Primary Health Centres from where the patients could be monitored. Distribution of contraceptive pills is being carried out from 1430 urban family planning centres, voluntary organisations and 691 Primary Health Centres. 104,000 lakh cycles of oral pills were despatched during the quarter April to June, 1975. Incomplete reports have been received up to May, 1975. Eighteen thousand six hundred and forty-one women were continuing the use of oral pills. This programme has not been very satisfactory and the number of users is very short of expectations. To spread the knowledge about oral contraceptives to the general public, it has been decided to advertise in the lay press. Manufacture of oral pills in the country is also being processed.

I. U. D. : The IUD programme has shown some improvement in 1975-76 with a total of 103778 insertions against 99,485 in 1974-75. The State of Assam has shown a very commendable performance showing an increase of 173.1 per cent over that of last year. One lakh CuT-200 are to be imported in 1975-76 of which 75,000 have arrived already. Sixty-five thousand CuT-200 have been distributed to the different States. CuT-200 has been found to be much more acceptable than the Lippes Loop.

Conventional Contraceptives : **Nirodh** is being distributed through (i) Commercial distribution (ii) Free Supply Scheme (iii) Depot Holder Scheme. The Scheme of **Nirodh** marketing was launched in September, 1968 with a view to create a large scale primary demand. The sale and distribution is being undertaken by seven of the country's largest consumer product companies. It is being further extended to other public enterprises like Oil India, Indian Durgs and Pharmaceuticals etc. The Central Government is responsible for the publicity and demand creation. The Scheme has shown better progress in the free supply scheme. Abuse of **Nirodh** distribution especially in the free scheme needs more vigilance. Assam has shown very good performance in 1975-76 showing an increase of 159.9 per cent compared to last year. In the overall performance Assam has performed exceedingly well in 1975-76 but as it was a backward State they still have a long way to go.

From the foregoing it is obvious that the Central Government has instituted every possible measure to boost the performance. With extensive facilities totally free and the enormous infrastructive, achievement of targets should not be difficult given the dedication and will to work. There are very few countries in the world today where all methods of fertility control are available with any cost. The medical profession with rapid advances in medical technology are largely responsible for the steep fall in death rates and the ensuing imbalance. Doctors must, therefore, consider it their sacred duty to reduce the birth rate if our country and future generations are to survive.

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Current Status of Contraceptive Technology

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Today mankind grapples with many great problems, such as peace or destruction, extension of political and economic freedom, improvement of standards of living, promotion of health, advancement of literacy. But the population problem is certainly high on this list. What exactly is the problem ? What are its origins and what are its consequences ? What is the role of science in the effort to resolve the problem ?

Despite all the startling numbers used to describe "the population explosion", the basic issue is not quantitative. The real problem is to keep the quality of human life. The problem derives from unprecedented population growth and the threat is not a number but a rate. India has been a pioneer in initiating an extensive programme of Family Planning as a national government undertaking. There are approximately 100 million couples in the reproductive age group in the country and to bring down the birth rate to the desired level of 30 per thousand by the end of the 5th Five Year Plan, 42 million couples must be covered with some method of contraception. As of October, 1975, the total coverage has been only 17.1 million, of which sterilization constitutes 13.23; conventional contraceptives 2.45 and Intra-Uterine Devices 1.42 million.

Research efforts in India and abroad are being intensified to develop newer techniques and improve existing methods of contraception. In the case of a new method, certain standard procedures have to be followed before the method can be made available for extensive use in the family planning programme. These include animal toxicological studies, Phase I-III clinical studies. All these investigations require at least 5 to 7 years and, therefore, in the context of the urgency of the problem, emphasis has to be given to the rapid improvement of existing methods.

Abstinence : It is not only an age-old method of contraception but is the only sure method for birth control. Practices such as celibacy, late marriage, long lactational period, taboos in relation to menstruation and child birth have promoted this method of contraception. Moreover, even as late as 1975, individuals are propogating devices for artificial intercourse.

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*Deputy Director General

Condom : Condoms have been used all over the world for centuries and the failure rate has varied from 17 to 40 per cent. In order to increase the acceptance of condoms, innovations such as lubrication and coloured condoms have been introduced. In addition, condoms made from polyurethane/ethylene ethyl acrilate are being investigated to evaluate the possibility of using condoms repeatedly.

Vaginal chemical contraceptives : Over 3000 years ago Egyptians used chemicals in the vagina for the purpose of contraception. Creams, jellies, suppositories, have been available for several years now and several innovations have been introduced. One of our national institutes, (Central Drug Research Institute, Lucknow) has also been promoting research in this field and has developed Cent-square (methyl Cellulose sheet containing urea/indigenous drugs). Acceptance of these devices as contraceptives is being investigated.

Vasectomy : The procedure of Vasectomy was introduced over a century ago, primarily for reducing complications from prostate operations and for promoting sexual rejuvination. As a family planning method, it has acquired great importance in our country's family planning programme. Newer methods, aiming at reversibility are being developed such as intra-vasal contraceptive devices, clips, valves, etc.

Sperm production : Inhibition of sperm production is another approach to the problem. Chemical compounds as medroxyprogesterone acetate and testosterone have been used for this purpose although some reports indicate decrease in libido. Attempts are presently being made to inhibit sperm maturation which would reduce the fertilizing capacity of spermatozoa. Drugs like cyproterone acetate are being evaluated for this purpose.

Ovulation inhibition : Inhibition of ovulation is another method of fertility control which has been fairly widely used over the past two decades. Ovulation inhibition has been achieved using a combination of steroids and the use of oral pills and injections is based on this principle.

Prediction of ovulation : Investigations are presently being undertaken to predict ovulation. These include 'Billing' method, cholestrol/oxygen concentration of the cervical mucus; temperature changes recorded with ordinary thermometer or thermosensitive devices. With the predication of ovulation conception can be prevented using the rhythm method.

While emphasis is on methods based on ovulation inhibition, several investigators have been concerned with major disturbances in the normal hypothalamo-pituitary physiology that is associated with it. Therefore, attempts are being made to develop methods which would not inhibit ovulation. Steroids are being given as oral pills, subdermal implants, vaginal rings, biodegradable material, skin contact aborption technique, intrauterine device release, nasal spray etc. The drug released acts at the peripheral target tissue level.

Tubal sterilization : Tubal sterilization is the main stay of our national programme and in fact, attempts are being made all over the country to popularise this further. One of the major deterring factor for the wider acceptance of this method has been its irreversibility. Attempts are presently being made to develop reversible methods for tubal occlusion. Trials with clips and chemicals are being carried out in this context. In addition, research is being undertaken to promote egg transport with drugs. The objective of these studies are to induce a disparity between the maturation of the egg and the recepient endometrium whereby implantation is prevented.

IUDs : Intrauterine devices have been used in the country for over a decade. The acceptance of the devices has varied in different States. While the method (IUD) has been accepted by some women, adverse publicity has promoted removal of the device for no obvious medical reason. Attempts have, therefore, been made to develop newer "Second generation" medicated intrauterine devices. The Copper IUD is now available in the national programme. Further improvements are being attempted to increase the life span of the device and reduce the expulsion rate. In addition copper devices for post-abortal and postpartum cases are also being developed.

Summary

1. There is an imperative need for rapid utilization of family planning services within next three years to achieve programme targets for reduction in birth rate.
2. It will take a minimum of atleast 5-7 years to develop newer methods.
3. International and national efforts have been intensified to improve/modify existing methods.
4. Scientific technology is important for development in contraceptive methodology.
5. Collaboration of medical researchers, chemists, agriculturists, mechanical engineers, etc. is essential.

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Health Aspects of Family Planning

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Family planning has often been defined simply as avoiding unwanted pregnancies but encompasses a large number of different activities. The latter depend on many conditions like socio-cultural factors, stage of technological development, standard and pattern of health services, demographic changes and reproductive performance. Fertility control is intimately related to economic development, maternal and perinatal morbidity and mortality and is mainly carried out by professional health workers and health organisations. The provision of family planning services is, therefore, of prime importance to medical and public health personnel. Education of birth control can be achieved by various methods like person to person communication, small group discussions, organised meetings and lectures, cinema slides and films. Both health worker and the general public would have to be educated on late marriage, timing, spacing and number of births which have been observed to have a profound effect on the health of the community. By identifying and contacting eligible couples and individuals, education regarding responsible parenthood, sexuality its social and ethical aspects, their personal health and welfare particularly that of their children can be inculcated and practised. Infertility can be investigated and treated. High parity is commonly associated with low socio-economic status, poor nutrition and hygiene, over-crowding, illiteracy and ignorance. The latter in turn go hand in hand with a high incidence of prematurity, difficult labour, dysmaturity trauma and infection.

Interruption of pregnancies perhaps provides the clearest indication for unwanted pregnancy for medical personal or social reasons. When abortions are carried out legally related mortality and morbidity is generally very low on a short term basis. Termination of pregnancy outside the medical setting is associated with most dangerous consequences of unwanted pregnancy Therefore, causes of abortion, circumstances of procurement need extensive and detailed studies. According to the Shah Committee 3.9 million criminal abortions occur annually in our country and 20 per cent of the maternal mortality can be ascribed to clandestine abortions. The single girl and her illegitimate pregnancy pose an enormous health problem both for the mother and her unborn child. Direct questioning in one of our hospitals revealed that eighty-two per cent of all births were unplanned and fifty-five per cent of the new born unwanted, maternal mortality which is the least in second pregnancy rises with each delivery after the third and then increases significantly after the fifth. Complications associated with pregnancy and labour have shown a statistical association with high parity. Placenta praevia, accidental haemorrhage, post-partum haemorrhage, prematurity prolapse of the cord and rupture of the uterus have a strong association with grand-multiparity nutritional deficiencies like severe anaemia, hypoproteinemia, osteomalaesia are often found in grand-multiparae. Increasing infant death rates are common with births of an increasing order. Some studies have indicated that children from smaller families have a higher quotient of intelligence. Certain birth control procedures may produce side effects which have a direct impact on the health of the individual.

Community development can be greatly accelerated when development staff, Panchayat leaders, Village Pradhans and Cooperatives are actively involved in family planning activities. Maternity services whether hospital or home-based form an ideal setting for propagating fertility control as the women in the post-partum period are easily motivated. Individual attention and continuity of care between the health workers and women and her family is generated leading to improved health and well-being. High priority should be given to women with one birth or more since this helps with timing and spacing of pregnancies. This would effect the health of the largest number of children yet to be born. By singling out high parity women as the main target group the demographic impact is very limited and consequently health benefits greatly diluted.

Inter-relation of many factors is responsible for human misery at one extreme or well.being at the other sustained high fertility produces a population that is demographically young and homes crowded with children. Such over-crowding is usually associated with poor nutrition inadequate environmental sanitation and rapid dissemination of infection. Children are likely to be under nourished succumb easily to inter current diseases. Health services are grossly inadequate and infant mortality high. Under these circumstances parents resist attempts at fertility control and additional children impose a further liability thus creating a vicious circle and further deterioration of health. Thus though death control in the short run leads to more rapid population growth in the long run it is a pre-requisite to increased acceptance of family planning. A number of studies have shown that couples are likely not only to compensate for children who have died but often tend to over compensate. However, an approach by integrating family planning with basic comprehensive health care and development is likely to have a much better chance of success.

It is clear that many factors reinforce each other. The most controversial of these have been the oral contraceptives for which the death rate has been computed to be approximately 3 for 100,000. Where, however, maternal mortality is high as in developing countries the risk to birth control methods is even less significant.

Family Planning care can be divided into 3 phases—contact, starting and continuing care. Contact may take place in a wide variety of situations varying from a visit to a general health clinic, through a health discussion with the auxilliary nurse midwife or field worker to dissemination of information through a variety of media. The starting phase would be concerned with the individual's first use of a contraceptive procedure like vasectomy or tubal ligation. Continuing care involves follow-up services and renewal of contraceptive supplies through convenient channels. Family planning can be combined with maternal and child health care, nutrition, immunization and curative services. This in fact is the strategy adopted by the Government of India in the Fifth 5-year Plan to bring down the birth rate to 30 per thousand at the end of the Fifth Plan. The value of combining birth control with a maternity centered approach has been amply demonstrated by the post-partum programme which is at present functioning in 256 hospitals. Apart from the above family planning has also been combined with specific disease control programmes especially cervical and breast cancer. It has been felt in some countries that family planning could be more advantageously combined with general medical care in stead of being administered in isolation by upto-dating the target couple registers vital statistics and registration of births would be more meaningful. Family life education aimed at future parents can help reduce illegitimate pregnancies many of which terminate so disastrously. It is therefore impossible to employ a single solution, as numerous activities must be coordinated. By identifying high priority areas family planning can be expected to vastly alleviated human suffering and contribute to the development of human health and happiness.

Ann Indian Acad Med Sci, 12, 4, Oct-Dec 1976

Health Services for Women

E. V. Sebastian*

Pioneering Efforts of Voluntary Organizations

Attention to the health of women appears to have been drawn during the latter half of 19th and the beginning of the 20th century on account of the prevailing conditions of child-birth in the country. Women who observed **purda** would not go to general hospitals and take medical assistance from men doctors. As no special facilities for giving medical care to women by women doctors were available in the country, the women faced great hardships and a large number of them lost their lives during child-birth. Many voluntary groups showed concern for the appalling conditions facing women during pregnancy and child-birth and organized themselves to take measures to improve the situation.

The Countess of Dufferin Fund

The earliest organized effort on an All-India basis to provide medical care to women appears to have been the formation of 'National Association for supplying female medical aid to women of India' under the patronage of Queen Victoria, the prospectus for which were issued at Simla on 18.8.1885 and circulated among the British Provinces and princely States. As set forth in the memorandum of the Association, the objectives for which it was established were :

(i) Medical tution including teaching and training in India of women as doctors; hospital attendants, nurses and midwives ;

(ii) Medical relief including (a) establishment under female superintendence of dispensaries and cottage hospitals for the treatment of women and children; (b) the opening of female wards under female superintendence in existing hospitals and dispensaries; (c) provision of female medical officers and attendants for existing female wards; (d) founding of hospitals for women where special funds are forthcoming.

(iii) The supply of trained female nurses and midwives for women and children's hospitals and private houses.

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The Association registered under the Societies Registration Act of 1860 and known by the name of "Countess of Dufferin Fund", pursued its objectives of establishing hospitals for women—Zanana Hospitals—called "Dufferin Hospitals" and providing scholarships for training of women doctors, nurses and midwives both within country and abroad for post-graduate studies till April 1948 when following the partition of the country the Central Council of the Association decided to dissolve itself and hand over its assets to the Red Cross Society in India and Pakistan. However, the share of the Central fund that came to India has been taken over by the Government of India vide the Countess Dufferin Act, 1957 passed by the Parliament of India. The share of the Bengal Province that came to the State of West Bengal has been taken over by that State Government through West Bengal Act XVI of 1955—The Lady Dufferin Victoria Zanana Hospital Act passed by the West Bengal Legislature.

Other voluntary associations like the Victoria Memorial Fund established in 1903 for improvement of the conditions of child-birth in India by training **dais**; the Lady Chemsford All India League for Maternity and Child Welfare founded in 1920 the Red Cross Society of India and its bureau for Maternity and Child Welfare started in January 1931 interested themselves in providing services for improving maternal and child health.

Women's Medical Service

With a view to improve the condition of services of women doctors serving in Dufferin Hospitals, a women's medical service was established by Countess Dufferin Fund in the year 1913 with a subsidy given by the Goverment of India. The original cadre strength of 25 officers was increased in 1924 to maintain a cadre of 43 senior officers and 25 training reserve officers. The women medical service officers manned 25 large hospitals including the Lady Hardinge Medical College in New Delhi and was in existence till 1948 when, after the partition of the country, it was disbanded. The members of the Cadre who opted to remain in India were absorbed on the strength of the Lady Hardinge Medical College and in the State Government Services.

Efforts by Official Health Agency

Besides the activities of the Voluntary Organisations, the governmental health agencies also showed considerable interest during the decade 1930-40 in Maternal health and the importance of child bearing contributing to female mortality. The report of the Public Health Commissioner for British India for the year 1936 showed that "during the age period 15-40 years, the female death rates were consistently higher than the male death rate and the greatest difference between the deaths occurred in the age period 20—30 years. It was assumed that child-bearing is a major factor which contributed either directly or indirectly or both to the different death rates in the two sexes."

Health Survey and Development Committee

The interest of the Government in the health problems culminated in the appointment of the Health Survey and Development Committee under the chairmanship of Sir Joseph Bhore in October 1943. The Committee known by the name of its chairman—"Bhore Committee" was required to make :

(a) Broad survey of the present position in regard to the health conditions and health organizations in India ; and

(b) Recommendations for further developments.

The report submitted in 1946 made special mention of the need for organising services for mothers and children. The report recorded; "the specially vulnerable groups in any community are the children, particularly those in the first year of life and old people. In addition, women at the reproductive ages are exposed to special risks during pregnancy and child-bearing and maternal morbidity and mortality are factors which require special consideration in estimating the state of public health". It also emphasised that "any plan for improving the health of the community must pay special attention to the development of measures for adequate health protection to mothers and children." The Committee further recommended that "Maternal and Child Welfare Organization will be an integral part of the general health service and is intended to provide domicilliary and institutional health protection for expectant and nursing mothers as well as for infants and children. In each local area, the same medical officers, public health nurse and midwife will deal with women during the ante-natal stage, confinement and the post-natal period. Similarly, the same staff will ensure the continuity of service to the growing infants throughout the period of child-hood."

Five-Year Plans : The Report of the Bhore Committee formed the basis for formulating the health plans for rural India in the First Five Year Plan. The philosophy of integrating preventive and curative services under one head, decentralising and taking them to the door steps of the people is realised in the Primary Health Centres and the sub-centres built up in the rural areas during the past four Five-Year Plans. Besides being responsible for the total health care of the community allotted to it, the Primary Health Centre gives special attention to the health needs of mothers and children. Regular advice and services for planning the family, ante-natal, natal and post-natal care of mothers and child health services are given through the Primary Health Centres for rural community. Services for children enrolled in schools and supplementary nutrition for mothers and children are also provided on a limited scale. Whereas in the rural areas, the Primary Health Centres provide integrated health services to the whole community including mothers and children, institutions catering only to women and children like Women and Children Hospitals, Maternity Homes and Maternal and Child Health Centres are built up in urban areas under the auspices of Municipal health organisations and Voluntary Organizations. The above mentioned types of institutions give gynaecological and obstetric services to women. The general medical and surgical problems of women are dealt with in the general hospitals in keeping with our philosophy of a unified and integrated system for delivery of health care.

Details of institutions providing services for mothers and children are given in Tables I and II.

Maternal Health Services

(i) **Ante-natal Services** : The Primary Health Centres and sub-centres, maternity hospitals, maternity homes, M. C. H. Centres etc. organise clinics for expectant mothers. Pregnant women are encouraged to register themselves at these clinics. Routine health supervision with specialised examination wherever indicated, treatment and corrections of deviations from normal health and health and nutrition education are provided at these clinics. In urban areas most mothers avail themselves of this service. However, in rural areas the proportion of mothers who receive ante-natal health supervision is small.

In addition to the clinic services at the institutions, the M. C. H. Personnel like the lady health visitors and Auxiliary Nurse-midwives provide domiciliary services. The home visits are used to identify mothers who are not registered at the clinics, to follow up the advice given to mothers at the clinics and to investigate cases of non-attendance at the clinics at the appointed time. Such visits enable the workers to assess the socio-economic status of mothers and its implication on the course of pregnancy and child-birth. Through such routine health supervision it is possible to identify mothers who have special health or obstetric problems and refer them to institutions for specialised care.

(ii) **Natal Services** : In the rural areas mothers prefer to have their deliveries in the homes and are mostly attended by unqualified persons. Only abnormal and

Table I. Existing facilities for Maternal and Child Health (Rural) as on 1. 9. 1975.

State/Union Territories	Provisional Rural Population as on 1.4.71 (in 1000)	C. D. Blocks	No. of PHCs functioning	No. of Sub-Centres	Other medical institutions
Andhra Pradesh	35,100	321	418	3014	38
Assam	13,336	130	121	440	460
Bihar	50,719	587	587	3,522	356
Gujarat	19,201	250	251	1,920	82
Haryana	8,264	83	89	743	96
Himachal Pradesh	3.219	69	76	273	525
Jammu & Kashmir	3,758	69	78	295	654
Kerala	17,881	148	163	1,761	254
Madhya Pradesh	34,869	457	457	3,271	1,355
Maharashtra	34,701	426	391	3,240	679
Karnataka	22,177	268	266	2,087	216
Orissa	20,099	314	314	2,038	316
Punjab	10,335	116	127	856	130
Rajasthan	21,222	232	232	1,624	447
Tamil Nadu	28,734	374	379	3,009	18
Uttar Pradesh	75,953	875	875	7,000	NA
West Bengal	33,345	335	298	1,512	5
Meghalaya	865	24	14	40	—
Nagaland	465	21	10	41	1
A & N Islands	89	5	3	3	1
Chandigarh	24	1	1	5	5
D & N Haveli	74	2	2	5	—
Delhi	419	5	8	34	40
Goa, Daman & Diu	631	12	15	51	31
LMA Islands	32	7	7	—	9
Manipur	931	26	16	47	10
Arunachal Pradesh	450	42	79	—	6
Pondicherry	273	12	11	33	36
Tripura	1,394	17	26	133	—
Mizoram	295	NA	3	18	—
Total :	438,856	5,224	5,317	36,997	5,780

Table II. Existing facilities for Maternal and Child Health Services (Urban)

Name of State/ Union Territory	Urban Popu. as per 1971 (in 1000)	Urban FP Centres	M. C. H. Centres *	Mater-nity Homes *	Mater-nity Hosp.	Mat. wards in Gen. Hosp.*	Child-ren Hosps *	Child-rens wards in Gen.* Hosp.	No. of Mat. beds *	No. of children beds. *
Andhra Pradesh	8,403	195	168	19	21	50	10	31	1,482	73
Assam	1,289	24	9	2	1	5	—	—	273	87
Bihar	5,634	93	51	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Gujarat	7,497	151	79	53	43	53	1	8	3,465	448
Haryana	1,773	36	22	—	28	21	—	2	528	60
J & K	858	14	5	—	—	6	—	4	150	100
Kerala	3,466	33	69	—	6	148	—	69	3,153	1192
Madhya Pradesh	6,785	102	42	25	15	139	1	18	2,491	256
Maharashtra	15,711	211	59	192	43	76	2	101	3,999	1343
Karnataka	7,122	56	7	27	11	121	1	45	3,570	667
Orissa	1,845	52	23	4	1	49	1	11	1,158	242
Punjab	3,216	33	53	5	8	17	1	14	929	685
Rajasthan	4,544	63	19	—	3	43	—	22	3,165	542
Tamil Nadu	12,465	243	241	82	8	215	1	44	2136	400
Uttar Pradesh	12389	214	133	34	199	146	1	13	7818	609
West Bengal	10,967	103	167	30	13	84	6	21	6,381	1271

Contd.

Name of State/ Union Territory	Urban Popu. as per 1971 (in 1000)	Urban FP Centres	M. C. H. Centres *	Maternity Homes *	Maternity Hosp,	Mat. wards in Gen. Hosp.*	Children Hosps. *	Childrens' wards in Gen.* Hosp.	No. of Mat. beds *	No. of children Beds. *
Nagaland	51	—	—	—	—	21	—	—	64	—
A & N Islands	26	—	1	—	—	1	—	2	38	44
Delhi	3,647	62	85	6	2	10	1	9	560	520
Goa, Daman & Diu	227	4	—	16	—	14	—	3	715	130
Himachal Pradesh	242	22	16	—	—	—	—	6	107	—
LMA Islands	No urban area		—	—	—	—	—	—	—	—
Manipur	142	4	1	1	—	1	—	1	15	6
Pondicherry	198	1	3	—	2	2	—	2	388	78
Tripura	162	2	6	—	—	—	—	—	—	—
Arunachal Pradesh	17	2	—	—	—	—	—	—	—	—
D & N Haveli	No urban area		—	—	—	—	—	—	—	—
Chandigarh	233	—	—	—	—	—	—	—	—	—
Meghalaya	147	3	—	—	—	—	—	—	—	—
Mizoram	4	1	—	—	—	—	—	—	—	—
Total	10,90,938	1,919	1,319	496	404	1,226	26	426	47,606	9,353

*Provisional figures.

complicated cases are taken to the Primary Health Centres and hospitals. In contract to this the trend in urban areas is towards institutional delivery. In the large Municipal Corporations almost 90 per cent of deliveries take place in maternity hospitals, maternity homes and private nursing homes In the urban areas, the over-crowded and inadequate housing conditions, the nuclear family system and the working status of women, etc. necessitate that they seek services of institutions for normal child-birth.

In keeping with the need of the community, the Primary Health Centre provides services for home deliveries through its Auxiliary Nurse-midwives and lady health visitors. The Maternal and Child Health Personnel visit mothers in the homes and make preparations for confining them in the homes provided normal delivery is expected. In municipal areas also the midwives of the Maternal and Child Health Centre and Maternity Home will delivery mothers in homes if so desired.

(iii) **Post-natal Services :** Mothers delivered in the homes by dais and M.C.H. personnel are given post-natal care in the homes to start with. They are encouraged to visit the post-natal clinic at the Primary Health Centre/M.C H. Centre six weeks after delivery for physical check up and family planning advice and service.

(iv) **Gynaecological Services** : Women's Hospitals also have sections for gynaecological diseases. Special clinics are run for screening women for cancer of cervix and other diseases peculiar to women.

Child Health Services

As the large majority of child-births takes place in homes, the immediate care of the new-born baby is given by the Aux-Nurse-Midwife or the dai who attended on the mother. They follow up the growth and development of infant by advising the mother on the needs of the growing infant, specially its nutrition needs. Mothers are encouraged to breast-feed the infant during the first year of its life supplemented with suitable solid foods after four to six months of age.

Immunisations against small-pox, tuberculosis, diphtheria, whooping cough and tetanus are provided to children routinely. Immunisation against poliomyelitis, typhoid and cholera are given when indicated, Supplements of minerals and vitamins, proteins and calories to combat nutritional deficiency diseases widely prevalent among children are also provided.

Primary Health Centres and Children Hospitals run special clinics for monitoring the growth and development of normal children and providing the required immunisations and nutritional supplements. However, this facility is not availed of by mothers to the extent they should. Generally, mothers take chidren to the hospitals when they are ill and not for preventive and promotional services. The proportion of children who receive all the routine immunisation is small.

Special facilities for the treatment of children diseases are built up in the district headquarters hospitals and the Medical College teaching hospitals under specialist paediatricians. The general practitioners look after children in the smaller hospitals and primary health centres and refer those having special problems to paediatricians.

Special Schemes for Maternal and Child Health sponsored by the Ministry of Health & Family Planning

The basic health care programme described above is provided by the State Goverments. The Government of India, the Ministery of Health and Family Planning have sponsored special schemes for promoting the health of mothers and children through the Five Year Plans. These Schemes included training of traditional birth-attendants (**dais**); training of health visitors, auxiliary nurse-midwives; establishment of maternal and child health centres in backward areas etc.

The schemes for the training of Lady Health Visitors, Auxiliary Nurse-Midwives and traditional Birth-attendants have been taken into the Department of Family Planning from the Fourth Plan onwards and is continued in the current Plan. In addition, new schemes for immunising children agains diphtheria, pertussis and tetanus, immunising pregnant mothers against tetanus ; proyhylaxis against nutritional anaemia among mothers and children and prophylaxis against Vitamin A deficiency diseases among children have been sponsored by the Department of Family Planning during the IVth Plan period and are continued in the current Plan.

(i) **Immunisation of children against diphtheria, whooping cough and tetanus** : As the Family Planning Programme is vitally interested in the health of mothers and children and as the State Governments had not taken up Schemes for immunising children against the above mentioned diseases, the Department of Family Planning sponsored a Scheme for the same. Funds were provided by the Family Planning Department and the immunisations are done through the health infra-structure in the States; in the rural areas through the Primary Health Centres and in the urban areas through the children's clinics of the different kinds of institutions of both Government and Voluntary Organizations.

(ii) **Immunisation of pregnant mothers against tetanus :** Pregnant mothers are given tetanus toxoid with a view to protect them from peurperal tetanus which may follow the midwifery practices of untrained dais and to give protection to the new-born infant against tetanus neonatorum which is a major cause of infant deaths in many parts of the country.

(iii) **Prophylaxis against Vitamin 'A' deficiency diseases among children :** Nutritional status surveys have brought out the high degree of prevalence of Vitamin 'A' deficience diseases among children. The inadequate availability of foods rich in Vitamim 'A' as well as ignorance and poverty contribute towards this. As a short-term measure to combat Vitamin 'A' deficiency diseases among children a Scheme has been evolved to administer a dose of 2 lakh I.U. of vitamin A in oil by mouth once in every six months to children between 1 and 5 years of age. The Scheme is implemented in nutritionally backward areas where the deficiency of vitamin 'A' is considered to be high. The workers from the P.H. Centre visit the homes and give the Vitamin A solution in the mouths of children.

(iv) **Prophylaxis against nutritional anaemia among mothers and children:** Nutritional anaemia among women and children has emerged as a major public health problem. Efforts are made to control this by giving mothers and children a tablet containing the daily requirement of iron and folic acid, the deficiency of which in diet is considered to be cause for anaemia. The tablets are distributed to pregnant and nursing mothers, women who have accepted family planning and children through the mother and child clinics of P.H. Centres and hospitals.

(v) **Training of Traditional Birth Attendants (Dais) :** The objective of the Scheme is to give elementary knowledge about midwifery and family planning to women who practice midwifery without any formal training as a family profession handed down from mother to daughter. The training is conducted at the Primary Health Centres and sub-centres. The dai is required to attend the Centre once a week and the training is spread over a period of six months. She is paid rupees ten per day of attendance at the P.H.C. to meet expenses of travel, food, etc. On completion of the training each dai is provided with a midwifery kit After the training, she works closely with the Aux-Nurse-Midwife of the P.H.C. and sub-centres. She is entitled to a payment of rupees 2 for every pregnant mother she registers with the A.N.M. and whose delivery is reported to her. Despite the financial incentives the Scheme has not attracted many practising dais to take the training. It has received a low priority with the Health Administrators in the States and the pace of training has been slow. An outlay of Rs. 40 lakhs is indicated in the Fifth Plan to train 25,000 dais.

The scheme started during the Fourth Plan is continued in the Fifth Plan. The targets and the achievements for the Fourth Plan are given in Table III.

Table III. IV Plan - Special M. C. H. Schemes

Scheme	Targets - (figures in lakhs)		Achievement	
	Financial Outlay	Beneficiaries to be covered	Financial	Beneficiaries covered*
Triple Immunisations for children	25.00	73.60	22.96	40.70
Tetanus Immunisation for pregnant mothers		13.08		10.00
Prophylaxis against blindness caused by Vit. A. deficiency diseases in children	40.00	133.00	40.00	55.41
Prophylaxis against nutritional anaeaia - mothers and children.	200.00	182.30	124.37	144.51
Training of traditional birth attendants	50.00	0.40	N.A.**	0.0757

*The information is incomplete.
**The expenditure was incurred in the State sector.

The infrastructure available for rendering the services described in the preceding paragraphs is given below.

Teaching Hospitals of Medical Colleges
Women's Hospitals
Children's Hospitals

Urban Towns

Children's and Women's Hospitals
Women/Wing of General Hospitals
Maternity Homes
M. C. H. Centres
Nursing Homes
Private Practitioners

Rural Villages

P. H. Centres
Sub-Centres
Dispensaries
Dais
Private Practitioners

Administrative Organisation : Health is a State subject. However, the Government of India in the Ministry of Health and Family Planning exercises advisory and regulatory function. The Bureau for Materniy and Child Welfare under an Adviser established in the Directorate General of Health Services in the year 1948 was transferred to the newly created Department of Family Planning in the year 1967.

At the State level a Bureau for Maternal and Child Health and Family Planning functions in the Directorate of Health Services, generally under a joint or Deputy Director of Health Services. Within this Bureau an officer of the rank of an Assistant Director is given the specific responsibility for Maternal and Child Health Services. The general medical care services for women is looked after by the Officer-in-charge of medical care in most States.

At the District level the Chief Medical and Health Officer is in overall charge of health programmes. A Deputy Chief Medical Officer is assigned for Family Planning and M. C. H. Programmes. In some States a Public Health Nurse assists this Officer.

In the N. E. S. B. Block, the M. O. in-charge of the P. H. C. is responsible for all health programmes for women. The L. M. O. if available, PHN/L. H. V. assists him. At the sub-centre the Aux-Nurse-Midwife is responsible for looking after the health of women and children.

The Health Organisation has the primary responsibility for providing services for women. However, other Government departments like the local-self Government—Panchayats and Municipal, Social Welfare, Education and Rural Development are also involved in varying degrees.

The draft Vth Plan has defined its primary objective in the area of Health and Nutrition as 'providing minimum health facilities integrated with family planning and nutrition for vulnerable groups—children, pregnant women and lactating mothers. The strategy is to consolidate past gains in the various fields of health such as communicable diseases, medical education and provision of infrastructure in the rural areas; and increasingly to integrate family planning services with health, maternal and child health and nutrition activities. All these measures influence the health of women and children. We have come quite some way from where we started twentyfive years ago in providing health facilities for women (Table IV). But we have many more Plans to go through before we can hope to ensure optimum health for women in this country.

Table IV.

Physical facilities	Number 1950-51	Number 1960-61	Number 1965-66	Number 70-71	Number 74-75
Primary Health Centre	0	2665	4796	5044	5288
Sub-Centres	0	N. A.	13072	29178	33370
M. C. H. Centres	1700	7471	8900	8492	7173
Maternity Beds	10000	2859	45077	47606	47606
Children beds	N. A.	5012	8393	9353	8353
Manpower Resources					
Doctors	56000	70000	86000	115723	138000
Nurses	15000	27000	45000	71000	10000
A. N. M. Midwives	8000	19000	36000	57000	92000
Lady Health Visitor.	521	3161	4239	5933	9933

N. A.—Not available.

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Rapporteur's Report III

Report of Scientific Session III — Family Planning

Chairman : Dr. B. G. Kotwani

Rapporteur : Dr. Kamla Gopal Rao

Current Status of Contraceptive Technology

by Dr. S. Tejuja

Dr. Tejuja in her paper emphasised the need for looking upon the problem of population explosion as an issue in maintaining the quality of human life. She mentioned that in order to achieve the birth rate of 30 per 1000 by the end of 5th Five Year Plan, 42 million couples must be covered with some method of contraceptive while up to October 1975, the total coverage has been only 17.1 million. She discussed the research efforts in India and abroad to develop newer techniques of contraception and to improve the existing methods and highlighted the need for concentrating on rapid improvement of existing methods, as finding out new methods would atleast require five to seven years, and the problem is very urgent. She further discussed the latest innovations in the condom, such as, lubrication, colour condom and condom made from other materials. Discussing about vaginal chemical contraceptives, she mentioned the Cent Square that is being developed by the Central Drug Research Institute. Discussing the importance of Vasectomy in the family planning programme, she mentioned the newer methods aiming at reversibility, such as, Intra Vasal contraceptive device, clips, valves, etc. Other researches on inhibition of sperm production were also discussed and also mention was made of attempts to inhibit sperm maturation.

In the field of researches on Ovulation, inhibition of ovulation was mentioned to have been achieved using a combination of Steroids and oral pills and injectables. Other researches in this area are concentrated on prediction of ovulation, inhibition of ovulation, etc. Tubal sterilization as a method of contraception has gained considerable popularity in India and present research attempts are concentrated on development of reversible methods, promotion of egg transport, etc. The problem associated with the acceptance of IUD were discussed and attempts being made to develop the second-generation medicated IUDs and the copper IUD were mentioned. In the end she emphasised the need for collaboration of medical researchers, chemists, agriculturists, mechanical engineers, etc. in the research on contraceptive technology.

Rapporteur's Report III

Current Status of the National Family Planning Programme - its needs, objectives and effects

by

Dr. (Mrs.) A. Dass

The initial part of the paper reviews the population situation in India in the context of the overall problem in the world, discusses the causes for rapid increase in population and its consequences for the individual and the nation. Further on the paper discusses the objectives and focus of the family planning programme in India in in the different Five Year Plans, the organisational structure and performance of the programme. There is also a very close review of the different components and strategies in the programme, such as, the inputs in mass communication, special programmes, like the Hospital Post partum programme, medical termination of pregnancy, Oral pill programme, Conventional contraceptives, etc. She presented a critical review of the highlights in the development of the Family Planning Programme, changing strategies, changing policies, problems in achieving the demographic goals, performance in different States, acceptability of different methods and the reduction in birth rate achieved as a result of all these efforts. She also discussed in great detail the organisational structure and changes in the programme ever since its inception, their rationale and their impact.

In her second paper on 'Health Aspects of Family Planning', Dr. Dass discussed the health aspects of family planning in various dimensions. She particularly highlighted the health implications of late marriage, timing, spacing and number of births and the need for educating eligible couples and individuals regarding responsible parenthood, sexuality, their personal health and the health of their children. She also discussed the relationship between poverty and high parity and the complications thereon, such as poor nutrition, poor environmental hygiene and over-crowding, illiteracy and ignorance. She also traced the relationship of these to the high incidence of pre-maturity, difficult labour, infection etc. Later on she discussed the magnitude of the problem of induced abortion, particularly criminal abortions conducted by illegal abortionists and their undesirable consequences for the mother and their unborn child. She also pointed out that according to a Hospital Inquiry, 82 per cent of all births were unplanned and 55 per cent of the new born unwanted maternal mortality increases significantly after the 5th delivery. The complications associated with higher parity were discussed. The impact of birth control procedures in terms of side effects were also discussed. As a solution to all these problems, she suggested that Community Development Staff and Panchayat leaders, Village Pradhans and cooperatives can help a lot in the promotion of family planning activities. The need for concentrating on women with one birth to inculcate the idea of timing and spacing of pregnancy was emphasised. The adverse health consequences of sustained high fertility was also discussed. She particularly highlighted crowding, overpopulation and the resultant poor nutrition, inadequate environmental sanitation and rapid spread of infection. The close relationship between high levels of infant mortality and high fertility was discussed and the need for comprehensive health care services through integrated approach was highlighted. She divided the family planning care into three phases - contact, starting and continuing care. Further she discussed the strategy employed by Government of India in the 5th Five Year Plan where the emphasis is on combining family planning with maternal and child health care, nutrition, immunization and curative services. The value of combining birth control with a maternity centrered approach was discussed in the context of the post-partum programme currently operating in 256 hospitals. Apart from this, family planning has also been combined with specific disease control programmes, particularly with cervical and breast cancer.

Health Services for Women

by

Dr. (Mrs) E.V. Sebastian

In her paper on 'Health Services for Women', Dr. Sebastian traced the history of several efforts of voluntary organisations ever since the later half of 19th and beginning of the 20th century. The earlier efforts, such as, the Countess of Dufferin Fund, the Red Cross Society, the Women Medical Service were discussed. The efforts of official health agencies in improving the Maternal and Child Health were reviewed and recommendations of different committees, such as, the Health Survey and Development Committee and the different services for Women and Children under the Five Year Plans was critically reviewed. She gave a very detailed description of the different components of Maternal health services, such as, ante-natal services, natal services, post natal service and Gynaecological services. The organisational, functional and implementation aspects of these services were listed in great detail.

Coming to child health services, she mentioned about the immunization programmes, food supplement programmes and disease control programmes. Later she discussed the special scheme for maternal and child health sponsored by the Ministry

Session IV

Special Health Problems of Women

Ann Indian Acad Med Sci, 12, 4, Oct-Dec 1976

The Problem of Cervical and Mammary Cancer in India

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Cancer has become a universal public health problem within the past decade. The extensive statistical and epidemiological data emanating from western countries indicate that a consistent and progressive increase in its incidence and mortality occurs with the passage of time. To-day, cancer has thus become the second commonest cause of death in the West and to control the disease special efforts are called for.

To assess and specify the magnitude of the problem posed by the disease, an essential prerequisite is the availability of accurate morbidity and mortality data. Unfortunately, except for the information available at the Cancer Registry in Bombay, we do not have such information from any other specific population group in our country. Even though death registers are maintained in a number of urban centres, there is considerable scope for improving their quality and the methodology employed for registration before they can be used meaningfully, to assess the mortality incidence from cancer, with a reasonable degree of accuracy.

In our country, the usefulness of mortality statistics from any chosen area, remains limited, since the necessary data concerning a specific disease entity tends to be deficient. The information obtained from clinical records of patients attending hospitals can only reveal proportional rates or frequency ratios i.e. the number of patients affected by a disease, expressed as a proportion of all cases or of selected sub-groups.

Uptill the early 1950s, infant mortality, pneumonia, malaria, tuberculosis and infectious diseases used to claim dubious distinction in ranking, in public health tables. But during the past 15 years or so, a fair amount of control has been achieved over these traditional scourges and with this changing scene, chronic and degenerative diseases such as heart diseases and cancer have each begun to show a relative increase in incidence and are rapidly surfacing as ominous public health problems.

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*Director

**Coordinating Biostatistician, Bombay Cancer Registry, Indian Cancer Society.

We shall now talk on some of the conspicuous results obtained from the recent epidemiological studies undertaken by us on breast and cervical cancers in Greater Bombay, based on :-

(i) Hospital Statistics;

(ii) Area-wise Mortality Studies ; and

(iii) Area-wise Morbidity Studies.

Hospital Statistics

Recently, at the Records Department of the Tata Memorial Hospital, we initiated an exercise, in collaboration with the Bombay Cancer Registry, to analyse the data obtained on all cancer cases seen at some of the major hospitals throughout India. So far we have been able to obtain frequency ratios from 42 hospitals in 15 States and from 2 Union territories.

Table I presents the relative ratios of breast and cervix cancer cases as compared with all other sites in females as seen at these hospitals. Wide variations were noticed in the relative frequecency with which these cancers are seen throughout the country. Thus cervix cancer shows a frequency variation of, from 4.8 per cent to 62.6 per cent (average of 33.7 per cent), and breast cancer from 8.3 per cent to 29.2 per cent (average of 18.8 per cent).

Data based on hospital records suffer from obvious biases. However, considering the Bombay Cancer Registry figures as standard, being derived from a known population at risk, the relative frequencies are seen to be 21.7 per cent and 16.6 per cent for cervix and breast cancers respectively. It is, therefore, very unlikely that the frequency ratios based on hospital records are, unduly biased. In fact, female breast and uterine cervix cancers are the most prevalent form of cancers among Indian women throughout the country.

Total Mortality

The death registration system in Greater Bombay may be considered satisfactory. This situation is mainly due to the availability of fairly good medical facilities. In Greater Bombay, for example, the doctor population ratio is about 1 to 750. No dead body can be disposed of without a death certificate from a competent medical officer. All cancer deaths in Bombay have to be certified by qualified doctors.

Table I. Proportion of breast and cervix cases found in 100 cancer cases all sites in females seen at various States in India (1970-72)

State	No. of hospitals	Proportion of All cancer in female (140-209)	% of female Breast (174)	% of female Cervix (180)
Bombay Cancer Registry	Population based	41.4	16.6	21.7
Maharashtra	10	39.2	16.5	32.4
Uttar Pradesh	3	59.4	8.3	62.6
New Delhi	3	54.5	16.4	29.7
Himachal Pradesh	1	39.6	14.5	20.6
Punjab	1	60.4	16.2	40.5
Madhya Pradesh	1	50.3	13.6	52.9
Rajasthan	1	59.0	29.2	29.5
Gujarat	2	30.1	16.3	30.9
Bihar	1	34.4	26.0	32.2
Orissa	2	47.4	13.3	39.9
Tamil Nadu	3	49.2	10.8	39.0
Kerala	2	41.6	20.1	4.8
Karnataka	5	51.7	8.9	46.7
Andhra Pradesh	3	59.8	11.9	41.8
Calcutta	2	39.7	12.5	47.2
Assam	1	22.6	8.3	18.3
Pondicherry	1	48.1	8.4	41.5

During a 9 year period, from 1964 to 1972, 17,215 (10,448 males, 6,767 females) resident cancer deaths were certified by qualified doctors in Bombay. Every year cancer takes a toll of approximately 4.3 per cent (2.6 per cent males, 1.7 per cent females) of all deaths occuring in the Metropolis.

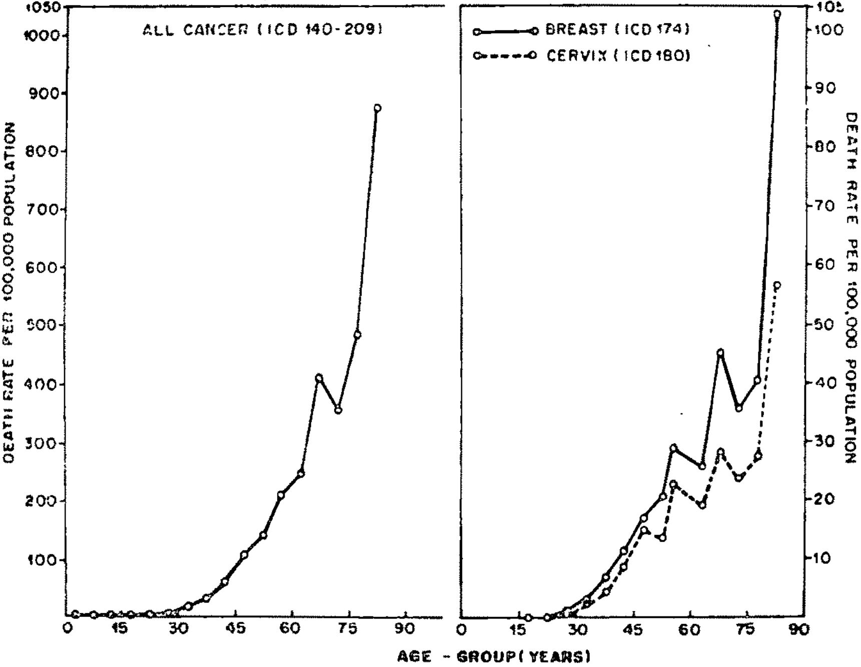
In 1971, cancer was the 9th leading cause of death in women, with breast and uterine cervix cancers taking the maximum toll.

Three important factors that influence the mortality rate of breast and cervix cancers in Greater Bombay, are age, sex and religion.

Figure 1 compares the age specific mortality curves for breast and cervix with all cancers, in females. Such age-specific death rates confirm that an increase in incidence occurs with age, the mortality being comparatively higher for breast cancer. The age-adjusted death rates are found to be 9.2 and 6.6 per 100,000 population per annum respectively, for breast and cervix cancers. For all cancers taken together the age-adjusted death rates are 91.0 and 73.7 per 100,000 for males and females respectively.

Figure 1

AGE-SPECIFIC DEATH RATES OF BREAST (174), CERVIX (180) AND TOTAL CANCER (140-209) PER ANNUM / 100,000 FEMALE RESIDENT POPULATION, GREATER BOMBAY, 1964-1972

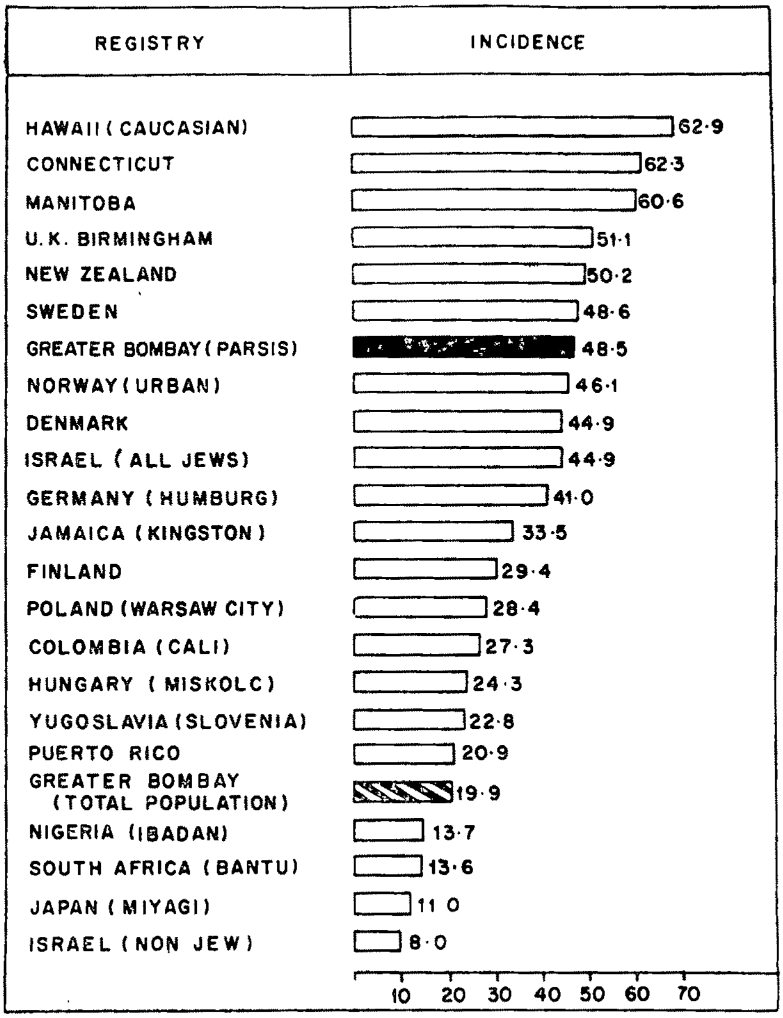


Parsi women present uniformly high mortality rates (144.2 per 100,000) for all forms of cancer, compared to the experience of women from other religious communities (e.g. Hindus 33.0, Muslims 35.8, Christian 48 1, Buddhists 32.4 and Jains 12.0), as shown in Table II.

Total Morbidity

To assess and specify the problems posed by various types of cancers, a cancer registry was established in June 1963 as a unit of the Indian Cancer Society at Bombay, in a precisely defined urban area (Greater Bombay) and regular compilation of epidemiological data then became possible from the year 1964. Until that year, no precise epidemiological surveys, in a chosen population at risk, had been undertaken in our country, on a continuing basis.

Figure 2



AGE-ADJUSTED (WORLD) INCIDENCE RATES FOR CANCER OF THE FEMALE BREAST FOR VARIOUS REGISTRIES. DATA FOR VARIOUS REGISTRIES, EXCEPT OF GREATER BOMBAY, DERIVED FROM 'CANCER INCIDENCE IN FIVE CONTINENTS', (UICC, 1970).

Table IV. Average annual incidence of female breast cancer per 100,000 population among Parsis and other religions, Greater Bombay, 1964-1972.

Religion	Annual incidence per 100,000 population	
	Crude	Age-adjusted*
Parsis	77.1	48.5
Others**	10.1	18.2
All	11.1	19.9

*Adjusted to world population (UICC, 1970).
**Hindus, Muslims, Christians, Sikhs and Jains.

Figure 2 compares the breast cancer incidence rates in selected countries. The age-adjusted (world) breast cancer incidence, for all religions taken together, is 19.9 per 100,000 per annum. This rate is relatively low in Greater Bombay and close to the figures reported from Puerto Rico and Yugoslavia (Slovenia). Populations in South Africa (Bantu), Japan (Miyagi Prefecture) and Israel (Non-Jews) present even lower rates than in Greater Bombay. On the other hand, populations in Hawaii (Caucasians) and USA (Connecticut) have incidence rates 3 times higher than at Bombay.

Two-thirds of the present world population of Parsis (about 64,667 in number at the time of the 1971 census) live in Bombay, (where they constitute about 1.1 per cent of the city's population), and present an age pyramid remarkably different from that of the population of the city as a whole, as can be clearly seen from Figure 3. Owing to their small numbers and strict religious rules against marrying outside their own sect, they have been in a sense, inbred for more than two millennia. In fact, Parsi women carry a 2.7 times higher risk from breast cancer than the rest of the population of Bombay.

In Figure 4 the age-specific curves for Parsi women and other religious communities are examined. The breast cancer age-specific curves for Parsi women and other religious communities show an increasing trend with age. Parsi women seem to get breast cancer later - mainly in the third decade, followed by an increase in incidence upto the ages 40-44, a slight drop in incidence is then seen in the age-group 45-49, after which there is a study rise once again. On the whole the incidence rates tend to follow the general pattern of increase with age.

women being 16.9, in Muslims 12.0, in Christians 9.1, in Parsis 6.4, in Buddhists 16.0, in Jains 2.8 and in Sikhs 11.2 per 100,000 population per annum, 1970-72.

Cancer of the uterine cervix appears to be predominantly a disease of married women, occurring particularly in those who marry at an early age and immediately bear a large number of children. The incidence of cervical cancer in these women (24.4 per 100,000) vastly exceeds the rate noted in spinsters (7.5 per 100,000), as shown in Table III. Whatever influence marital status, active sexual life and child-bearing may have on the development of cervical cancer, the suspected factors (traumatic, infective or hormonal) begin to exert their action at a much earlier age many decades before final effect is seen. There is a vast difference between the mean ages at marriage (14.4 year), at first delivery (18.7 year) and at last delivery (29.5 year) - when the suspect factor is believed to begin its action - and the mean age at which cancer finally seems to arise (46.4 years). It appears that uterine cervix cancer arises as a result of numerous early pregnancies and frequent coitus, but only after a prolonged latent period, before revealing its presence.

Table III. Age adjusted rates, per 100,000 population, of cervical cancer by marital status, Greater Bombay (1964-66).

Marital status	Age adjusted rate per 100,000 population
Unmarried	7.5
Married	24.4
Widowed	24.9
Divorced	.29.3

Prevention of cervical cancer as of all other cancers is basically dependent upon early detection and identification of the ancillary aetiological factors responsible as the direct cause for the cancer is not yet known. A practical and useful approach, to control cervical cancer in our country is to combine cancer detection with family planning activities. This is a simple, easy and practical way to achieve an important objective without spending an appreciable amount of money.

Incidence of female breast cancer : The breast is the second commonest site involved by cancer in Indian women. It is interesting to note in Table IV that the Parsi women of Greater Bombay have a remarkably high age-adjusted (world) incidence of cancer at this site i.e. 48.5 per 100,000 as compared to other communities in whom the incidence is 18.2 per 100,000.

Table II. Average annual crude death rate of cancer per 100,000 population by religious communities in resident women of Greater Bombay, 1964-1972.

Religion	Average annual crude death rate per 100,000 population
Hindus	33.0
Muslims	35.8
Christians	48.1
Parsis	144.2
Buddhists	32.4
Jains	12.0
Others	50.8
Total	35.4

During the period between 1964 to 1972, the Bombay Cancer Registry recorded a total number of 31,867 cancer cases, at all sites. Of these, 59.7 per cent (19,020) were males and 40.3 per cent (12, 847) females. A total of 2,783 (21.7 per cent) women were found to have had uterine cervix cancer and 2,130 (16.6 per cent) breast cancer.

Incidence of Cervical Cancer : Although cancer of the cervix uteri occurs at all ages, it is mainly observed during middle age. An increase in the age-specific rates is first observed around the age of 25, followed by a steady increase upto the age group 50-54. Thereafter an apparent decline is noticed. In fact, most registers throughout the world report this rise in incidence of cervical cancer around the age of 30.

The cervix is the leading site involved by cancer in Greater Bombay females and accounts for approximately one-fifth the total female cancer recorded. The average annual age-adjusted (world) incidence rate, was 23.9 per 100,000 during 1970-72, for this site, which assumes intermediate ranking in international comparison.

The crude incidence rate of uterine cervix cancer in Greater Bombay women differs considerably in various religious communities. The incidence in Hindu

Figure 3

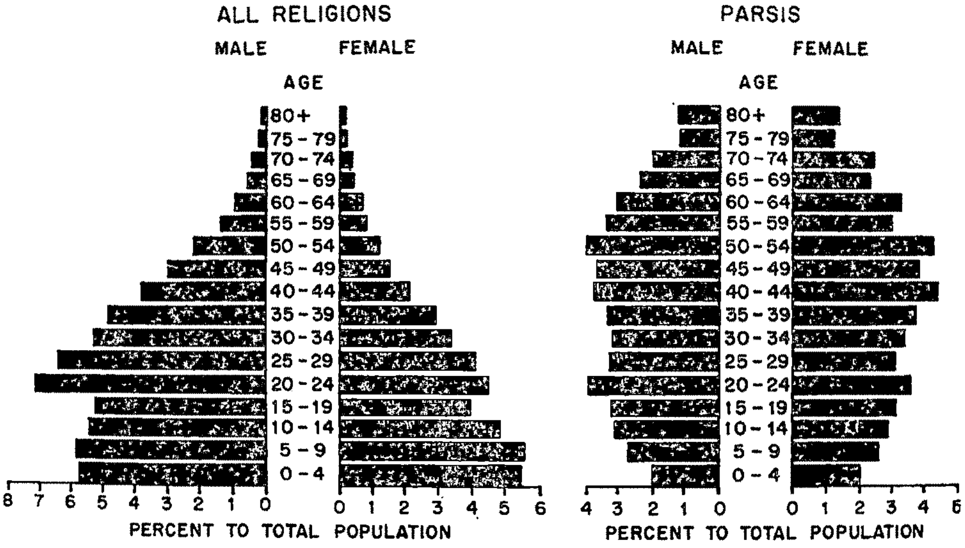


FIG. — ESTIMATED AVERAGE RESIDENT POPULATION FOR ALL RELIGIONS AND PARSIS IN GREATER BOMBAY AS ON 1ST JULY, 1971.

Among 2,130 female breast cancer cases, 80.7 per cent were married and only 6.2 per cent unmarried, as shown in Table V.

Table V. Proportion of breast cancer cases by marital status and religion, Greater Bombay, 1964-1972.

	Marital Status			
Religion	Unmarried	Ever married*	Not known	Total
Hindus	2.1	50.2	6.8	59.1
Muslims	0.9	11.8	1.7	14.4
Christians	1.6	8.9	1.9	12.4
Parsi	1.5	6.9	2.3	10.6
Buddhists	—	1.0	0.2	1.2
Jains	0.0	1.0	0.1	1.2
Others	0.1	0.8	0.1	1.1
Total	6.2	80.7	13.1	100.0

*Married, Widowed, Divorced and Separated.

Figure 4

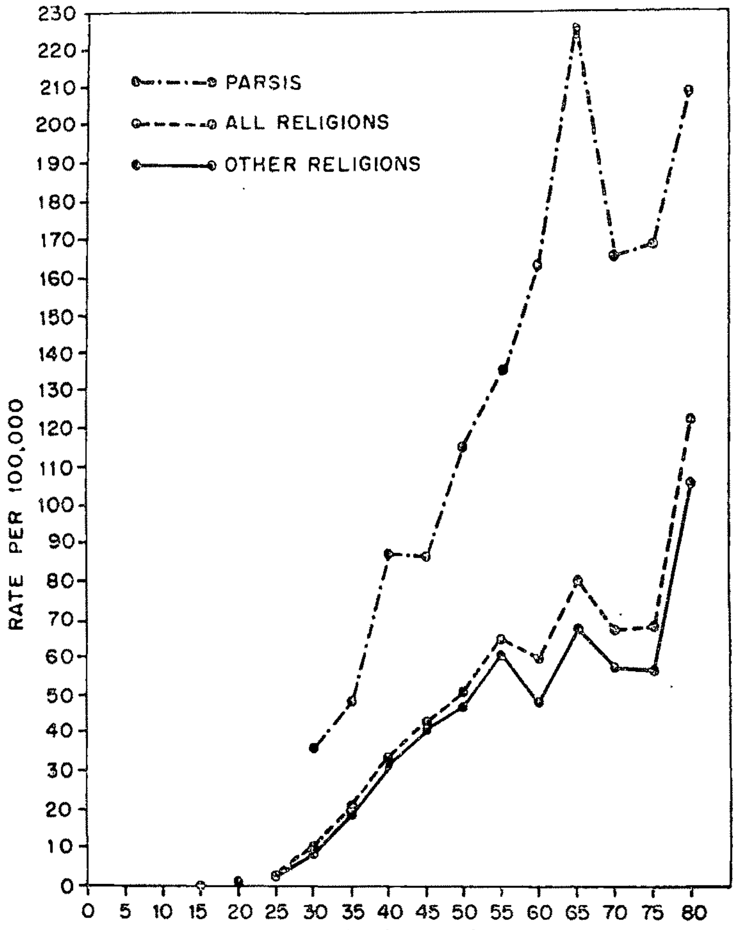


FIG. - AVERAGE ANNUAL INCIDENCE PER 100,000 BY AGE IN PARSIS AND OTHER RELIGIONS IN GREATER BOMBAY, 1964-1972.

An average of 3.4 children per woman in 2,130 breast cancer cases were observed, with the exception of Parsi women, in whom the average is only 2.7 children per woman (Table VI).

Table VI. Average number of children in 2,130 female breast cancer cases by religion in Greater Bombay, 1964—1972.

Religion	Average number of children
Hindus	3.3
Muslims	3.8
Christians	3.3
Parsi	2.7
Buddhists	3.2
Jains	4.9
Others	4.7
All religions	3.4

In fact, the low parity Parsis carry a high risk of breast cancer and a low risk of uterine cervix cancer while other communities show the reverse phenomenon.

We have so far discussed only the epidemiological aspects of breast cancer. However, many factors seem to influence breast cancer development. Experimental studies have shown that diet is possibly a factor in breast cancer development. Restricted diet has greatly reduced mammary tumour incidence in mice (Tannenbaum and Silverstone, 1959). For high-tumour strains, simply reducing the food supply significantly decreases the mammary tumour incidence, but there are no data showing that variations in diet affect breast cancer rates in humans.

Recently, investigations on tumour viruses have also given hopes of preventing cancer in man. Both DNA and RNA viruses are implicated in human cancer etiology. The RNA virus has now been identified as the milk factor of Bittner that has since 1936 been associated with carcinoma of the mammary gland in mice and is now highly suspect of the etiology of breast cancer in women.

In collaboration with Dr. Dan Moore* and his associates at New Jersey, studies at our Centre have identified a "B" virus-like particle in milk samples, drawn from normal Parsi women. Further studies are under way and milk and tissue samples from Parsi women are under going ultra-microscopic studies. Strangely,

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*American Cancer Society Research Professor and Head of the Department of Cytological Biophysics at the Institute for Medical Research, New Jersey.

"B" particles are more frequently seen in the milk obtained from Parsi women than in North American women (under investigation by Dan Moore and others) even though the American women are at comparatively higher risk. We are at present engaged in undertaking DNA-RNA hybridisation, utilising human milk samples and breast cancer tissues, of Parsi and non-Parsi Indian women. These studies appear to provide significant indication by implicating the "B" particle as one of the factors involved in the causation of human breast cancer.

Experimental studies of virus-induced mammary tumours in mice may perhaps lead to prevention of breast cancer in humans, by leading to the development of a vaccine.

Reference

Tannenbaum, A. and Silverstone, H. 1959. Nutrition and the genetics of tumours. In **Cancer**, 1, R. W. Raven, ed. London : Butterworth, pp. 306—334.

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Problem of Carcinoma of Cervix

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Age adjusted death rates for malignant neoplasms from four countries are shown in Table I. Figures from India are taken from the Bombay Cancer Registry. It would be seen that the problem of cancer in India is no less than in other developed countries.

The age specific incidence rates per 100,000 population, for various sites, sub-sites and sex for the period 1967-69 are shown graphically in Graph 1. The age specific rates follow the general pattern of increase with age. The rate of increase is gradual for the first four decades, but shows a sharp spurt in the older age groups in both the sexes. This is of relevance in view of the increase in the average life span of an Indian to over 50 years during the last two decades.

Comparison of the common forms of cancer, ranked by age adjusted rates during the year 1964-66 and 1967-69 is shown in Graph 2. As would be seen, cancer of the cervix takes the top rank followed by the breast. Similar figures are available from hospital statistics, from various parts of the country, wherein cancer of the cervix accounts for 20 to 50 per cent of all neoplasms. The variations in the frequencies from different parts of the country are not clearly understood. Derived incidence rates from a study on prevalence and distribution of cancer of the uterine cervix in Agra District, indicates Agra among population of highest risk for cervical cancer in the world.

It is further interesting to see that of all the tumours of the female genital tract, cancer of the cervix nearly constitute 3/4 (i.e. 72.5 per cent) of the total bulk of female genital tumours (Table II).

The natural history of cancer of the uterine cervix is still not clearly understood. There is evidence that cancer of the uterine cervix does not arise from a normal epithelium but is preceded by a spectrum of epithelial abnormalities which are termed as "epithelial dysplastic lesions", Early recognition and detection of these lesions with adequate treatment will considerably help in reducing the morbidity and mortality due to cervical cancer. Even prevention has become a distinct possibility with the institution of population screening programme.

Table I. Age adjusted death rates for malignant neoplasm.

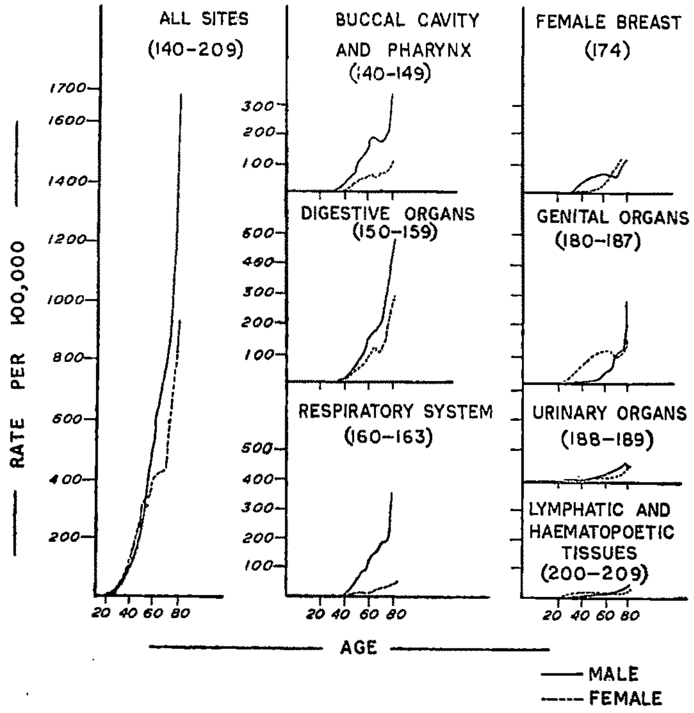
(Rates per 100,000 population)

Countries	Male	Female
England	180.3	114.7
U. S. A. (White)	143.0	104.5
U. S. A. (Non-white)	166.1	119.5
Japan	140.2	94.7
India	141.9	118.4
(Bombay Cancer Registry)		

Ref: Segi **et al** Metal : Cancer mortality for selected sites in 24 countries - No. 5 (1964-65).

Graph 1.

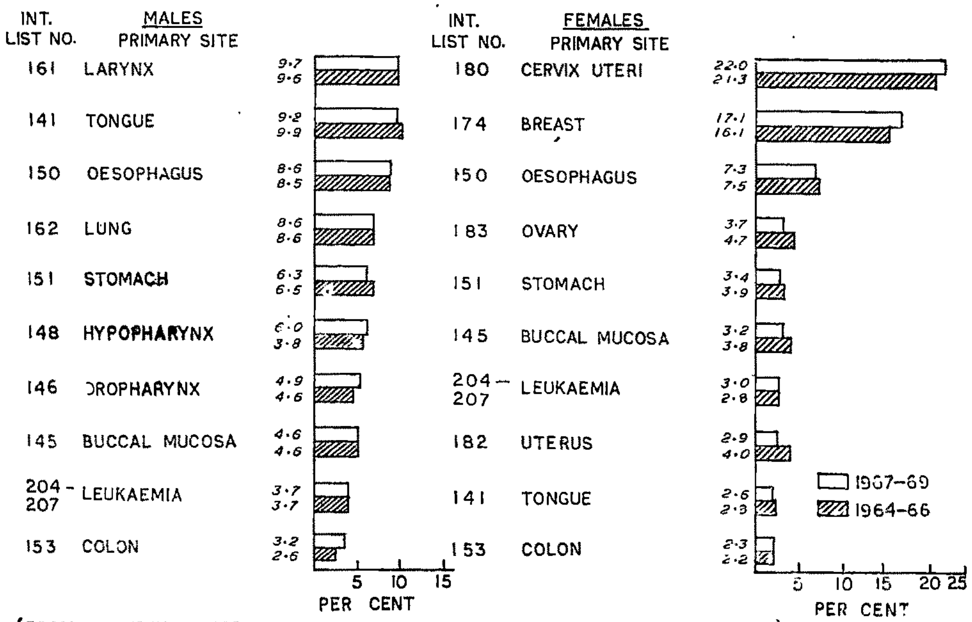
AGE SPECIFIC INCIDENCE RATES BY SEX, AND SITE-GROUPS, 1967-69



(FROM BOMBAY CANCER REGISTRY OF THE INDIAN CANCER SOCIETY)

Graph 2.

COMPARISON OF THE COMMON FORMS OF CANCER, SEEN DURING THE PERIODS 1967–69 AND 1964–66



(FROM BOMBAY CANCER REGISTRY OF THE INDIAN CANCER SOCIETY, 1967–69)

Table II. Percentage distribution of female genital tract tumours—site-wise.

(Bombay Cancer Registry 1967-69).

Number of cases	Sites of female genital tract							
	Cervix Uteri		Uterus		Ovary		Vagina & Vulva	
	No.	%	No.	%	No.	%	No.	%
1,247	904	72.5	136	10.9	150	12.0	57	4.6

Role of certain environmental factors in association with cervical carcinoma has been described. These can give an important lead in preventive oncology if put into practice.

Some sporadic hospital studies and population based studies at Bombay and Agra have been carried out to investigate these environmental factors in relation to cervical cancer in Indian women Two recent studies, one a collaborative study on hospital case control material from centres at Delhi, Madras and Bombay and the other field study from Delhi urban population were undertaken by the Council. The final analysis of these studies is under processing.

I would briefly highlight the results of a PL-480 project to study the prevalence and role of various environmental factors associated with cervical cancer in urban and rural areas of district of Agra carried out during 1967-70. Prof. Wahi was the Chief investigator of the study during the earlier part. Others who participated in the study were Dr. Mali and Dr. (Mrs) Lahiri. The results of this study are fairly representative as to the relation of various environmental factors to cervical cancer as reported from other parts of the country.

This study revealed that prevalence rate of cervical cancer increases as age advances. Muslim females had 1/2 times low prevalence rate of cervical cancer than Hindu females. Major difference in prevalence rates between these two religious groups could be subscribed to circumcision only. Uterine cervix cancer patients had married earlier and had produced more children as compared to healthy control woman.

It would be of interest to note that more or less similar environmental factors were related to cases of cervical dysplasia as that for cases of cervical carcinoma. The most frequent clinical diagnosis in these cases was cervical ulcers and cervical erosion. Majority presented with a history of contact bleeding and blood-stained discharge. Cases of severe dysplasia were more frequent in Hindus, a trend similar to cervical cancer. There was an increase in the occurrence of cervical dysplasia by age. Cases with uterine cervical dysplasia had married earlier and had like cases of uterine cervical cancer produced more children as compared to healthy control women.

The exact significance of these dysplastic lesions and their role in the pathogenesis of cervical cancer still remains obscure. Probably they represent an intermediatory lesions between inflammatory lesions and cervical carcinoma. The biological behaviour of these lesions shows a fluctuating nature. There is substantial evidence to suggest that if left alone some of them will regress while others may persist or progress to higher grades of dysplasia or even to malignancy. Dysplastic lesions, therefore, need a careful follow-up for prolonged period.

Use of Contraceptive: In recent years and rightly so, more and more women are being motivated to the use of contraceptive devices. Several controversial reports have appeared in world literature as to whether or not the use of varied types of contraceptives have any relation with cervical carcinoma. Because of the long latent period in the process of carcinogenesis to various environmental agents, a long-term follow-up with adequate monitoring of the subjects is a must before any opinion can be expressed.

We are conducting cytological monitoring in women using various contraceptive devices alongwith clinical trials at the Contraceptive Testing Unit. Two thousand three hundred and sixty-seven women have been registered for long-term use of Cu-IUD and have so far been followed up for a maximum period of 42 months. Analysis of the data has not shown any significant increase of precancerous or cancerous morphological changes during this period of follow up. However, in view of the remark made above and also that a sizable number of women revealed an inflammatory preinsertional smear, the biological behaviour of this group vis-a-vis the group of users with a negative initial smear needs to be followed up.

Cervical cancer control : Since the cause of cervical cancer is still not known, efforts should be directed to check its progression and prevent complications by early detection through cytological screening before observable abnormalities and clinical symptoms become apparent.

We know that risk of developing cervical cancer is more in women of low-socio-economic status and those who marry early and have multiple pregnancies. Women attending the family planning clinics are important subjects for the study. Attention should thus be concentrated on these high-risk groups. Total protection i. e. adequate detection services, treatment and follow up is the key to a successful cervical cancer control programme. The goal of the programme should be to prevent deaths from uterine cervical cancer through the integration of cervical cytological studies into the existing medical care systems and family planning programme to serve the women at risk. This would with minimum inputs (approximately Rs. 2.60 paisa per woman per test) save duplication of funds and offer a positive service to the women at risk and those attending the family planning programmes.

Cytological screening programme : The largest and the best known cytological screening programme has been the one undertaken at the British Columbia, where approximately 3/4th of female population of 20 years and over, have been screened. There has been a distinct drop in the incidence of clinical carcinoma in the population screened and it would now appear that the mortality is dropping as well

Two cytological screening programmes were undertaken in Agra, one during 1960-63, covering nearly 39,000 women and the other in 1967-70, covering nearly 26,000 women. It is of interest when the results of the two studies are compared. In the second study, the number of cancer cases have gone down while the number of women with dysplastic lesions has gone up significantly as compared to the first study. The positive search for cancer cases by household visit resulted in detection of early lesions which would have otherwise advanced if it was left to the patients to seek advice for clinical symptoms.

Ann Indian Acad Med Sci, 12, 4, Oct—Dec 1976

Problems of Heart Disease in Women

S. Padmavati* and R. Arora**

Maulana Azad Medical College and Associated Irwin and G. B. Pant Hospitals, New Delhi, India

Among school children there was a higher prevalence of rheumatic and congenital heart disease in boys than in girls. Hospital admissions showed a large proportion of male admissions inspite of an equal number of beds. There were a large number of male cases for all types of heart disease being least for rheumatic and highest for coronary heart disease. These findings are somewhat different from those reported in Western countries. There was a 0.9 per cent incidence of heart disease among pregnant patients in Delhi. Rheumatic heart disease formed the bulk of these cases (82 per cent). Death occurred in 5 per cent of pregnant cardiac women. Inspite of a lower admission rate, death from rheumatic heart disease formed nearly half of total deaths and cor-pulmonale a quarter, in women. This points to the importance of heart disease as a cause of death among women.

Introduction

Diseases of the cardiovascular system account for one out of two deaths in persons over 40 years of age in affluent countries (Paul, 1971) and outstrips cancer and infections as a cause of death. While the figures for India are not known with certainty, there is an increasing incidence of heart attacks, strokes and deaths from rheumatic heart disease seen in hospitals throughout India. This paper relates to the relative mortality and morbidity from heart disease in women in India.

Material and Methods

Data from several sources have been drawn :

(1) School surveys in children between 5—16 year age group.

(2) A randomized secondary rheumatic fever prophylaxis programme involving young age groups.

(3) Hospital statistics from the Govind Ballabh Pant Hospital, New Delhi.

(4) Previous published data on heart disease and pregnancy.

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*Director and Consultant in Cardiology.

**Lecturer in Cardiology.

Results

The material has been analysed with reference to age and sex distribution and other related features.

Prevalence of heart disease in children : School children numbering 34, 198 ; 21, 209 (62 per cent) boys and 12, 989 (38 per cent) girls, in 5—16 year age group were screened in Delhi as part of a collaborative programme under the Indian Council of Medical Research involving five cities (Padmavati, 1972-75). Of 375 cases of rheumatic heart disease detected (11 per 1,000), 274 were boys (12.9 per 1,000) and 101 girls (7.9 per 1,000), There were 111 cases of congenital heart disease (3 per 1,000), 67 (60 per cent) were boys and 44 (40 per cent) girls. It is not clear, whether there was a greater frequency of rheumatic heart disease in boys as compared to girls in India or whether it was due to relatively fewer girls being examined, as they were shy of physical examination and very often refused to be examined. Out of 1318 randomized cases of rheumatic fever in persons below 20 years subjected to chemoprophylaxis between 1966-74, there were more boys (707, 53.6 per cent) than girls (611, 46.4 per cent) (Padmavati **et al** 1973). Most workers in this country have found rehumatic heart disease and particularly mitral stenosis to be more common in males (Roy **et al** 1963) in contrast to the findings from western countries (Paul, 1943).

In adults, however, Berry (1972) in a study of prevalence of chronic rheumatic heart disease in an urban community of 28, 249 persons of all age groups and found an incidence of 1.12 per 1,000 in men and 1.98 per 1,000 in women.

Hospital statistics : Of 5,004 cardiac cases admitted to Govind Ballabh Pant Hospital between 1971-75, there were 3,209 (64 per cent) males and 1,795 (36 per cent) females, although the number of beds are the same for the two sexes. It is customary in India for fewer women to seek admission, for various reasons e.g. indifference to health except when the disease is serious and general reluctance to enter the hospital.

Type of heart disease (Table I) : Rheumatic heart disease which accounted for the largest number showed a male preponderance for all types of valvular lesions. The male to female ratio for rheumatic heart disease was 1.2 : 1, for coronary artery disease 4 : 1 and for hypertension and congenital heart disease 1.5 : 1. This is again contrary to the data elsewhere, as hypertension is slightly more common in females and when all forms of congenital heart diseases are considered, the incidence is equally divided among the two sexes (Friedberg, 1969). When coronary artery disease cases were analysed according to the age spread (Table II), the largest number of males were between 51-60 years and females 61-70 years, a decade later. This is in keeping with what is found elsewhere (Peel, 1955). At all ages there was a male preponderance of this disease.

Table I. Types of Heart Disease in Hospital Admission (1971-1975).

	Male		Female		Total	
	No.	%	No.	%	No.	%
RHD	918	55	748	45	1666	33.2
CAD	1244	80.5	302	19.5	1546	30.8
Hypertension	280	60.6	182	39.4	462	9.2
Cong. HD	334	60.0	221	40.0	555	11.3
Miscellaneous	433	55.8	342	44.2	775	15.5
Total	3209		1795		5004	

Table II. Relationship of age and sex in CAD.

Age in Years	Male		Female	
	No.	%	No.	%
Below 30	11	1.3	0	—
31—40	144	16.35	28	14.4
41—50	161	18.94	26	13.7
51—60	281	33.06	42	21.6
61—70	160	18.93	67	34.2
Over 70	86	10.12	31	15 9
Total	843		194	

Heart disease as a cause of death : A large percentage of deaths in women were due to cardiovascular diseases e.g. 344 (36 per cent) out of 957 deaths in a study at Lady Hardinge Hospital, New Delhi (Padmavati and Kumari, 1967). Rheumatic heart disease accounted for 45 per cent and cor pulmonale for 24 per cent of fatal cases.

Pregnancy and heart disease : Previous publications by one of the authors while at Lady Hardinge Medical College, New Delhi, for women, showed that the incidence of heart disease was 0.9 per cent among 28,069 pregnant women seen in the hospital (Sood and Padmavati, 1965). Similar figures are reported from many other countries (Conradsson and Werko, 1974)—Australia 0.5 per cent, Vienna 0.7 per cent, Scandinavia 0.9 per cent in 22,000 pregnancies and slightly higher figures from United States around 2 per cent, the range being 1.2 to 3.7 per cent in different hospitals.

Rheumatic heart disease accounted for the largest number (82 per cent) in pregnant cardiac cases followed by congenital heart disease (8.7 per cent) and hypertension (7.2 per cent) in that order (Sood and Padmavati, 1965). Of the valvular lesions due to rheumatic heart disease, mitral stenosis was the commonest (60 per cent) followed by combined mitral stenosis and regurgitation (19 per cent) and the combined mitral and aortic lesions (15 per cent). The largest number of patients were between 20-29 years (70 per cent) and half of them had 1-3 children. Of serious complications, pulmonary oedema was the commonest (22 per cent) followed by congestive heart failure (13 per cent) artrial fibrillation (6 per cent), haemoptysis (5 per cent) and cerebral embolism. Rheumatic heart disease accounts for 85-95 per cent of total cardiac patients in most of the series reported (Sweet, 1962).

The importance of premarital examination is evident from these figures, as many young women die of pulmonary oedema during their first pregnancy.

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Ann Indian Acad Med Sci, 12, 4, Oct—Dec 1976

The Problems of Burns in Women

J. L. Gupta

Safdarjung Hospital, New Delhi

From times immemorial, social, martial, political, biological and certain other inequalities out of convention have kept the importance of women undermined. An unprejudiced analysis will reveal, that inspite of all this, women have always been creator of society's common boons. They have always helped to promote the progress of society and the mankind Today, as is generally known, women produce, almost a third of all benefits at the disposal of mankind. Proclamation of International Women's Year is clearly an acknowledgement of Women's steadily increasing importance in the modern society. The efforts of the Madam Prime Minister in our country for the uplift of women in society are so well known to all of us.

Women in a developing country like ours, are the main propulsive force of a family unit. This is much more appreciable, when one realises the fact, that she has expanded spectrum of her responsibilities from house-keeping, rearing children, looking after the husband and elders at home, to her active participation in the economic and political problems of a city, a state, and the country as such. Inspite of such a variety of responsibilities, physical and social looking after of women in our society is far from what it should be. Her health suffers in number of ways.

Spurts of Industry in India during the recent years has created a lot of health hazards and fire is one of them. More and more involvement of women in industry adds to her more exposure to hazards.

Overall incidence of burns in the country is not easily assessable because of lack of a central Registry for burns. However about 21936 cases of burns have received attention at the Deptt. of Burns, Plastic and Maxillofacial Surgery, Safdarjang Hospital, New Delhi, from 1964 to 1974. Children are the most common victims (9851) followed by females (6924) and then males (5161). Common causes of burns in our patients were:

(1) Flash and Flame from loose clothing catching fire, bursting of stoves, Petromax and spilling of kerosene oil.

(2) Scalds from hot liquids like milk, tea, ghee and boiling sugar cane juice etc.

(3) Electric burns.

(4) Chemical burns from acids and alkalies.

(5) Petrol fire.

(6) Coal-tar burns.

(7) Industrial burns from molten metals and rubber etc.

(8) Miscellaneous caused-cigarrettes, Plane crash, jhugi fire. and burns due to lack of sensations, as in leprosy and some neurological disorders.

Management of burns depends upon the percentage of body surface involved and depth of burns. Those patients who fall in the range of critical levels of shock are resuscitated in the intensive care unit with intravenous fluids, plasma and blood, analgesics, monitoring of pulse, blood pressure, intake/output charts and dressings.

In local treatment of burns, the eschar is left to auto separation which takes about 3 weeks. The wounds get ready for skin grafting only in about 4 weeks time and complete recovery takes about 6 to 9 weeks. Inspite of all advancements in antibiotics, systemic and topical, the burns today are attended with a very high death rate, high incidence of toxaemia, infection, septicaemia. Serious late sequele like disabling contractures deformities and disfigurements need subsequent rehabilitation of the patients

Invariably most of the causes, due to which burns accident occur, are preventable. It is suggested that some of the preventive measures like redesigning of kitchen, stoves, Petromax, safety lamps, improvisation of electrical gadgets, fitting of safety appliances to gas cylinder and discouring loose and nylon clothings in kitchen are adopted uniformally. Treating the thatch with chemicals before making jhugi roofs is a very welcome suggestion.

I am very confident that the subject of today will receive a very serious thought and as a result, a sustained campaign will be unleashed which would make life safer for women whether it is at home, office or factory.

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Rapporteur's Report IV

Report of Scientific Session IV—Special Health Problems of Women

Chairman : Dr. Shanti Ghosh

Rapporteur : Dr. Kamla Chandra

The IV Scientific session on 'Special health problems of women' began with Dr. Shanti Ghosh; Pediatric Consultant, Safdarjang Hospital, New Delhi in the chair.

The first paper on 'the problem of mammary cancer' dealt with both mammary and cervical cancer in India and was presented by Dr. D. J Jussawalla from Bombay. He gave a good statistical account of mammary and cervical uterine cancer in different communities of Greater Bombay. His paper was dealt with under three main headings (a) Hospital Statistics (b) Total Mortality statistics by cancer and (c) cancer morbidity statistics. The three main communities analysed in detail were Hindus, Parsis and Jains. Cervical cancer showed a frequency of 4.8 per cent to 62.6 per cent and breast cancer from 8.3 per cent to 29.2 per cent. Female breast and utrine cervix cancer are the most prevalent form of cancers among Indian women throughout the country. In 1971, cancer was the 9th leading cause of death in women with breast and uterine cervix cancers taking the maximum toll. During the period between 1964 to 1972, the Bombay Cancer Registry recorded 21.7 per cent uterine cancer cases and 16.9 per cent breast cancer cases of cancer at all sites. Cancer of the uterine cervix appears to be predominantly a disease of married women occurring particularly in those who marry at an early age and immediately bear a large number of children. The incidence of cervical cancer in these women (24.4 per 100,000) exceeds the rate noted in spinsters (7.5 per 100,000) The breast is the second commonest site involved by cancer in Indian women. It is interesting to note that Parsi women of Greater Bombay have remarkably high incidence of cancer at this site i.e. 48.5 per 100,000 as compared to other communities in whom the incidence is 18.2 per 100,000. Their data shows that contrary to the figure in Western literature married women had a higher incidence of breast cancer than unmarried ones. Experiments conducted by them on Female (Mice) showed a reduced incidence of mammary cancers with reduced intake of calories. However, there was no such co-relation seen in human beings. The RNA 'B' virus particle closely related to the Bittners' Milk Factor was seen more frequently in the milk of Parsi women as compared to American women who are reported to show the highest incidence of mammary cancer.

The second paper on 'the problems of cancinoma of the cervix' was presented by Dr. Usha Luthra, Deputy Director-General, I.C.M.R. Her observations were based on the studies conducted in and around Agra and Delhi covering both the urban and rural population. She reiterated the epidemiological factors related with carcinoma cervix and stressed upon the association of early marriages, early sexual relations and multiparity with the higher incidence of cancer cervix. She also brought out the point that cancer cervix was seen significantly more frequently in Hindu women as compared to Muslim women. She mentioned that this may probably be related to circumcision in Muslim men. Dr. Luthra said that cancer cervix does not arise in normal cervical epithelium but is always preceded by dysplastic changes of varying degree. The severer the dysplastic change the higher the risk of developing cancer was her contention. She stressed that screening of women in the high risk group would enable early detection of precancer and cancer of the cervix and thus help in eliminating the disease. Another pertinent comment was that the screening of women for cancer cervix should be coupled with the family planning programme. This will enable early detection of malignancy and will also serve the dual purpose of monitoring the use of contraceptive devices. They have calculated that this coupling of screening with the family planning programme would entail an additional cost of Rs. 2.60 only per capita.

The next paper on 'the problems of heart disease in women' was presented by Dr. S. Padmavati, Director of Maulana Azad Medical College complex and President of the Indian Academy of Medical Sciences. Her opening remark was the startling observation that 1 out of every 2 after 40 years of age in affluent groups died of heart disease. She brought out the high incidence of Rheumatic Heart Disease in school going children (375 RHD/40,000 children surveyed)—53.6 per cent of the rheumatics seen in boys and 46.4 per cent in girls. In the adult population incidence of heart disease was 1.29 per cent males and 0.79 per cent in females. Of the cardiac cases men suffered more frequently from heart disease (64 per cent in men and 36 per cent in women). Coronary heart disease was more frequently seen in men whereas Rheumatic heart disease was more frequently seen in women. Hypertension and corpulmonale etc. were seen with almost equal frequency in both males and females. Dr. Padmavati said that the lower serum cholesterol levels may be responsible for the lower incidence of ischaemic heart disease in women, also higher incidence of smoking and greater stress conditions in men may explain the higher incidence in men. Considering pregnant women Dr. Padmavati said 9 per cent of pregnant women had associated cardiac disease. Eighty-eight per cent were due to Rheumatic Heart disease. Mitral stenosis was the commonest lesion and Pulmonary oedema the commonest complication. The age group between 20-29 years showed the highest incidence. Dr. Padmavati recommended that all women should be screened for mitral stenosis before marriage and corrective measures undertaken before the girl is permitted to marry.

The last paper of the session on 'Problems of Burns in Women' was presented by Dr. J L. Gupta from Safdarjang Hospital, New Delhi. He presented a lucid paper with illustrations on the incidence, cause and care of burns in women as encountered at the Safdarjang Hospital. Of the 22,000 cases of burns registered 7000 were in women, the highest number 9,800 being in children. Most of the cases were registered as accidential burns though a good many may have been due to suicidical burns.. Only two cases of homicidal burns were registered. Accidents were invariably preventable and were due to (a) badly designed kitchens, stoves, petromax, improvisation of electrical gadgets ; (b) Loose clothing particularly of synthetic material; and (c) Lack of safety appliances on gas cylinders and pressure cookers. A Skin Bank for plastic surgery was available at Burns Department, Safdarjang Hospital.

A short question hour followed wherein Dr. Padmavati and Dr. Gopalan asked questions. Answers have been included in the report.

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Report on the Indian Academy of Medical Sciences/Indian Council of Medical Research Seminar on "Health of Women" held at Maulana Azad Medical College on 23rd December, 1975.

During the International Women's Year, the National Committee (I. W. Y.), through its member, Dr. S. Padmavati, President, Indian Academy of Medical Sciences, urged to take such action as was necessary to identify areas of disabilities of women in the country are subject to and make suggestions for their removal and redress.

The President of the Indian Academy of Medical Sciences organised the Seminar on Health of Women under the joint auspices of the Indian Academy of Medical Sciences and the Indian Council of Medical Research with the support of the Ministry of Health, Government of India, on 23rd December, 1975.

The Seminar considered health of women under four broad topics :—

1. Demographic Aspects
2. Nutrition and Health Aspects
3. Family Planning
4. Special Health Problems of Women

The Seminar was inaugurated by Dr. C. Gopalan, Director-General, Indian Council of Medical Research, after the welcome address of Dr. S. Padmavati, President of the Academy. The President traced the history of the programme in the U. N. International Women's Year and drew the attention to the declining sex ratio, the age specific mortality in the female children and women and the various factors that are responsible for them, such as, ignorance, illiteracy, superstition, malnutrition and under-nutrition, repeated child bearing, lack of health facilities, descrimination, neglect in the society. She desired that the areas of research should be identified, guidelines for better development of health of women be made, to take speedy action.

Dr. C. Gopalan, Director-General, Indian Council of Medical Research, in his inaugural address observed that during the International Women's Year, the women's fight for human rights is commendable to play a legitimate role in all social, political and cultural activities. To achieve basic minimal levels of health is a fundamental need. As women form 50 per cent of the population, health of women has a direct bearing for the health of the population, which consists of 40-42 per cent children under the age of 14 and both men and children are to be nurtured, first for increasing productivity and second for developing future citizens. He emphasised the need for proper distribution of the available resources, particularly food for population and stressed the needs of the pregnant, growing children (below 5 years) and the rural poor. He desired maternal mortality and childhood mortality and the various factors behind them should be identified. He stressed the role of literacy in human development and the importance of health education. He gave the examples of Kerala and U. P. States with high rate literacy and low literacy rates respectively. He opined that maternal and child health services should be developed to give better coverage and the supplemental feeding programme for the pregnant and under five year aged children. He appealed to the Seminar to focus attention on the need for restoring the woman to her rightful place.

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Obituary

Prof. Sujoy B. Roy

Prof. Sujoy B. Roy was born in Burma. After completing a brilliant academic career in Rangoon University, he did his postgraduate work in Edinburgh and post-doctorate work in Boston, U.S.A. While he was working in Boston, on the faculty of Harvard University Medical School, late Raj Kumari Amrit Kaur, the then Minister of Health and President of the All-India Institute of Medical Sciences pursuaded him to come to India and take charge of the Department of Cardiology. Prof. Roy served the All-India Institute of Medical Sciences almost from its inception and by his persistent efforts built up an outstanding department of Cardiology. As Professor of Cardiology, he trained a number of young people to a high level of excellence and was responsible for bringing the spirit of scientific enquiry to the practice of cardiology infusing the students with excitement of discovery of the unknown.

Prof. Roy's studies on rheumatic fever and rheumatic heart disease have made a significant contribution to our understanding of the variance in the presentation, manifestation and other characteristics of this common disease in the developing countries. His research contributions in the field of high altitude cardiorespiratory problems are of very great value not only for the advancement of knowledge in this area but also for the light they throw on the health problems of great importance to our troups stationed at high altitude on our Himalayan borders.

He was elected Fellow of the Indian Academy of Medical Sciences in the year 1962. His various laurels include Padma Bhushan, Amir Chand Basanti Devi Award, Amalananda Award, Massachussetts Heart Fellow and FICCI Award 1976 for life sciences including agriculture. He was a member of the Armed Forces Medical Research Council and Cardiovascular Expert Committee of the World Health Organization. He contributed more than 150 papers to the learned journals.

— N. H. Keswani

Appeal

In memory of Late Prof. Sujoy B. Roy, the Faculty of the All-India Institute of Medical Sciences have established a fund called the 'Sujoy B. Roy Memorial Fund' which will be utilized for the promotion of patient care facilities in cardiovascular diseases, for financial support specially to the young scientists for carrying out research in cardio-vascular diseases, for promotion of exchange visits at individual and university levels and for the award of travelling fellowships, etc. You will appreciate that this requires generation of a large amount of finances, the proceeds of which should be sufficient to serve a worthwhile purpose. May we therefore appeal to you to make a generous personal contribution to the fund and request others also to do so. The cheques towards this donation may kindly be drawn in the name of "Director, AIIMS, New Delhi", which shall be entitled to income-tax exemption under Section 80 (g) of the Income-tax Act, 1961. A certificate to this effect will be provided along with the receipt for the donation by the Institute.

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Notice

NATIONAL BOARD OF EXAMINATIONS

Membership of the Academy of Medical Sciences, August, 1977

(Qualification included in First Schedule MCI Act, 1956)

Applications for the next MAMS examination to be held in August, 1977 will be received till 30th April, 1977 in the following specialities. Only medical graduates are eligible to apply.

1. **Division of Basic Medical Sciences** : Anatomy, Physiology, Pathology, Microbiology and Pharmacology.
2. **Division of Medicine & Allied Sciences** : General Medicine, Pediatrics, Psychiatry, Dermatology, Radio-diagnosis and Radio-therapy.
3. **Division of Surgery & Allied Sciences** : General Surgery, Orthopaedic Surgery, Ophthalmology, Anaesthesiology, Obstetrics & Gynaecology and Otorhinolaryngology.
4. **Division of Community Health** : Social & Preventive Medicine, Integrated Maternal Child Health Care, Health Administration including Hospital Administration, Health Education, Epidemiology, Occupational Health and General Practice.

The written examination may be held at different regional centres which will be announced later.

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Ann Natl Acad Med Sci (India), 13, 1, January—March 1977

Editorial

Transferable Drug Resistance

Antibiotics are one of the greatest benefits science has given to mankind. The premise of their discovery raised great hopes about victory over all pathogenic bacteria, but the development of resistance to the antibiotics and chemotherapeutic agents, as well as the toxic effects of some of them belied any such hopes. The development of resistance was shown to be due to genetic mutation. However, about twenty years ago a new kind of drug resistance—the transferable drug resistance was encountered. The transferable drug resistance has two disturbing features. It is multiple and usually concerns the drugs in common use, and can be selected by any antibiotic in the spectrum. Secondly the resistance could be transmitted from one bacterial strain to another by contact (bacterial conjugation). It has been mainly found in intestinal bacteria, pathogenic or non-pathogenic, of man and animals. This drug resistance is infectious and such strains have been known to have caused wide spread epidemics of dysentery, gastro-enteritis and typhoid fever in several parts of the world.

The properties of transferable drug resistance may be summarised as follows : The resistance may be to a single drug, but is usually multiple. The genetic element controlling the transferable resistance is the extra-chromosomal DNA elements (plasmid) and is designated as resistance factor or R factor. It consists of two components, the RTF (resistance transfer factor) and the genetic determinants for drug resistance; these must be in integrated form for transfer to occur. Transfer is effected by conjugation between the drug resistant donor cells and sensitive recepient cells, which may be of a different species. Such resistances transfer **en bloc** and can be selected by any single drug concerned in the 'R' factor. It has also been shown that organisms that had freshly received 'R' factors could transmit these with high frequency. Further characterisation of the 'R' factors can be carried out by transferring these to standard recepients and seeing the changes produced in the recepient cell e.g., fertility inhibition, restriction of action of phages, colicinogeny, compatibility with other plasmids and the DNA homology etc.

In 1957 for the first time the existence of R factor was demonstrated in shigellae in Japan. Since then transferable drug resistance has been reported in intestinal bacteria in many countries. In 1965 a large outbreak of infections due to

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*The views expressed in the editorial are the personal views of the writer and are not necessarily the views of the Academy.

S. typhimurium containing multi-drug-resistant 'R' factor occurred in U.K. Similarly 'R' factor containing **Shigella dysenteriae** caused a massive epidemic of bacillary dysentery in Mexico in 1969-70 causing about fifteen thousand deaths.

As early as 1968 Professor Anderson had warned against the use of chloramphenicol for conditions other than typhoid, predicting the emergence of chloramphenicol resistant typhoid organisms through the agency of the transferable drug resistance. His predictions came true when a serious outbreak of typhoid fever due to multi-drug-resistant **S. typhi** occurred in Mexico in early 1972. At about the same time an epidemic of typhoid fever due to chloramphenicol resistant 'R' factor carrying **S. typhi** occurred in Calicut in Kerala state. It followed in the wake of an epidemic of gastroenteritis due to enteropathogenic **E. coli** and shigellae, in which a combination of chloramphenicol and streptomycin was given on an unprecedented scale. According to Professor Anderson two conditions must pre-exit for appearance of epidemic strains carrying 'R' factors – (a) typhoid fever should be common in the area so that the bacillus is frequently present in the human intestine and (b) chloramphenicol should be used indiscriminately. Both such situations had prevailed in Kerala. The focus in Calicut has remained active since then. Last-year multi-drug resistant drug 'R' factor carrying **S. typhi** were encountered at Trivandrum, Bombay, Madurai and Ernakulam. Ernakulam is experiencing a prolonged outbreak of typhoid fever due to 'R' factor carrying **S typhi** since May 1976. The characters of 'R' factors in the typhoid bacilli from all these centres are similar, though different phage types were encountered.

R factors determining multi-drug resistance were also encountered in other salmonellae. In late 1975 and early 1976 more than two hundred strains of R factor carrying **Salmonella newport** were isolated from cases of neonatal septicemia in Delhi, having a high fatality rate. Similarly **S. paratyphi B, S. alachua, S. enteritidis, S. typhimurium** and **S. paratyphi A** carrying R factors were encountered at Bombay, Calcutta, Calicut, Manipal and Madras respectively. R factors have also been reported in shigellae, E. coli, Klebsiella from several parts of India, some of these in epidemic situations.

The increasing incidence of isolation of 'R' factor carrying intestinal pathogens is certainly an ominous sign. The risk to man does not depend only on transmission to man of drug resistant pathogens, but also on that of drug-resistant non-pathogenic intestinal bacteria, which must be abundantly communicated from animals to man, and such organisms get selected by the pressures of the indiscriminate use of antibiotics in not only human medicine but also in animal husbandry.

There has been much debate for the past several years on the potential danger of the increase of R factor carrying bacteria in animals as a result of antibiotic feeding. The Swann report (1968) from United Kingdom has recommended that use for animals of antibiotics which are being used as human medicines should be restricted and the use of antibiotics which cause an increase of 'R' factor—carrying bacteria or cross resistance to human antibiotic should not be used for animals.

The time has come to initiate a surveillance programme for transferable drug resistance to monitor appearance of new drug resistant pathogens and the prevalence of such pathogens in different parts of the country. It has also become essential to formulate a national antibiotic policy with regard to their use in human medicine, veterinary medicine and their use as growth factors in animal husbandry in the light of recommendations of the Swann Committee. Even in human medicine a rational approach to the use of antibiotics and chemotherapeutic agents in various conditions is necessary, since the discovery of new antimicrobial agents is becoming more and more difficult. It cannot be denied that the development of drug resistance casts dark shadows on chemotherapy as a whole. In this regard the medical and veterinary professions as well as the Pharmaceutical manufacturers bear a heavy responsibility. There has to be co-operative of all the three and the Government to evolve ways and means to reverse the change in the ecology of pathogenic enteric bacteria which has resulted today due to the injudicious use of antibiotics.

—K. B. SHARMA

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Fatal Traffic Accidents due to Motor Vehicle

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Received for publication, Oct. 31, 1975.

One hundred and two fatal traffic accidents have been studied. Agencies responsible for the accident, type of victim (Pedestrian, Vehicle, Occupant **etc.**) in relation to age, sex and incidence and distribution of injuries has been analysed and their significance is discussed.

Introduction

The incidence of fatal road accidents due to motor vehicle is on increase day by day with rapid development in transport industry, rapid increase in population, narrow roads and lack of traffic sense among the public.

Victims of fatal traffic accidents are the pedestrians, cyclists, motor cyclists, scooterists or the occupants of the vehicle. Pedestrian may receive injuries either by the primary or secondary impact injuries caused by the vehicle or secondary injuries caused by the victims striking other objects, such as the ground. Cyclist may receive injuries similar to these sustained by pedestrian except that the impact will be lower on the body or only against some part of bicycle itself. The secondary injuries will be more severe due to the greater distance to fall. The occupant (driver) will receive injuries on skin or hands **etc**. as he may take some of the force on his hands on steering wheel, thereby avoiding full impact in the chest or of the head against the wind shield, but from this he may receive injuries (fractures) of the wrist or forearms. Other occupants (passengers) may strike their heads against windshield or window frame or may sustain a fracture dislocation of cervical vertebrae due to impact or jerk (whip lash) (F. E. Camps 1968).

Material and Methods

The present paper is a study of fatal traffic accident cases that occurred during 1971-74. During this period 794 postmortems were done at Medical College Hospital, Aurangabad out of which 102 were of motor vehicle accident i.e. 12.8 per cent of total postmortem.

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There were 78 males and 24 females. Males made up about 4/5th of series (76.5 per cent) and females about 1/5th **i.e.** 23.5 per cent. The overall age and sex distribution is given in Table I. The maximum cases among the males were in age group of 20 to 30 years (24 cases) and among the females between age group of 0 to 10 years (10 cases)

Table—I. Age and Sex Distribution fatal road accidents.

Age group in years	Male	Female	Total
0 to 10	11	10	21
10 to 20	9	6	15
20 to 30	24	1	25
30 to 40	8	3	11
40 to 50	8	Nil	8
50 to 6o	12	2	14
60 to 70	6	2	8
Total	78	24	102

Maximum fatal accidents occurred in male in age group of 20 to 30 years as they are more exposed to accidents while in females maximum fatal accidents occurred in 0 to 10 age group **i.e.** in children. Incidence of fatal accidents in male children is also comparable with female children in age group of 0 to 10 years.

Table—II. Agencies responsible for fatal injuries in 102 traffic accidents.

Truck	71
Car	12
S. T. Bus	6
Tractor	2
Auto Rikshaw	4
Jeep	4
Tempo	3

Table—III. Incidence of injuries among the type of victim.

Pedestrian	78
Cyclists	6
Motor Cyclists	5
Occupants	13
(a) Occupant drivers	4
(b) Other occupants (Passengers)	9
Total	102

Distribution of injuries according to the different body areas affected in pedestrian subjects. Here only primary and secondary impact injuries and direct complications are emphasised. These are related to the major body areas affected i.e. head, chest, abdomen, pelvis, spine and extremities.

Table—IV. Incidence and percentage distribution of skeletal and visceral injuries, according to body areas in 91 subjects.

		Pedestrian 78		Motorists 13		Total	
		No.	%	No.	%	No.	%
Head :	Skeletal	40	51.2	4	30.7	44	48
	Brain	46	59	4	30.7	50	55
Chest :	Thoracic cage	15	19.2	6	46.0	21	23
	Pleura lungs	6	7.7	5	38.4	11	12
	Mediastinum	3	3.9	2	15.4	5	5
Abdomen :	Intestinal tract	2	2.5	1	7.7	3	3
	Visceral organs	10	12.8	3	23.1	13	14
Diaphragm :		3	3.9	Nil		3	3
Pelvis :	Skeletal	12	15.3	1	1.1	13	14
	Organs	3	3.9	Nil		3	3
Spine :	Skeletal	10	12.8	1	7.7	11	12
Extremities :	Upper	6	7.7	1	7.7	7	7.6
		8	10.2	2	15.4	10	10.8
	Lower	18	23.0	1	7.7	19	20.8

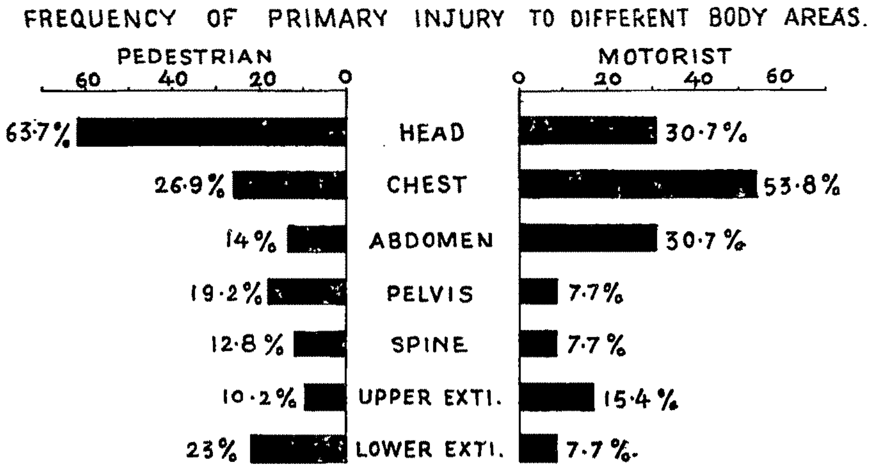
Note : All four drivers had thoracic cage injuries. Two had lung laceration and one had laceration of heart and rupture of aorta.

Table—V. Number of body areas involved in motor vehicle traffic accident fatalities in 78 cases(Pedestrian).

	Cases	Percentage
One body area	18	23
Two body areas	30	39.2
Three body areas	24	30.4
Four body areas	5	6.2
Five body areas	1	1.2

The Graph represents frequency rates of body involvement. Superficial, skin injuries, were disregarded in order to bring skeletal and internal lesions into sharper focus.

Graph



Comments

Most striking feature in this study is this. Head injuries rank all others among the pedestrian group while chest injuries are more frequent in motorists (occupants). All the four drivers had chest injuries. Driver may receive following injuries in a vehicle accident. The chest may strike the steering wheel and the sternum and ribs may be extensively fractured. In pedestrian the part of body involved right or left side, front or back will depend upon position of the person in relation to the vehicle when struck, namely whether struck when crossing the road from one side to the other or walking with or against the traffic. Position of injuries will depend on position of body and whether the feet are both on the ground or one is raised and the firmness or otherwise of either or both feet.

In post-mortem analytical study, it is not possible to give exact reconstruction of each injury though as a group the patterns of injury observed in the present study are in conformity with the findings of Jacob Kulowski (1960).

It is apparent from Table-IV that in regard to head region internal injuries are more frequent than the skeletal ones. This means that not infrequently internal injuries occur in the absence of concurrent fractures of overlying skeletal structures **i.e.** skull bones. In the present study brain injury was present more frequently than fracture of skull bones. This is in agreement with the findings reported by Jacob Kulowski (1960). Thus there were 6 per cent more intracranial injuries than skull and maxillofacial fractures. However in the present study skeletal injuries in the chest are more frequently seen than internal injuries unlike Jacob Kulowski's findings.

With respect to the pelvis which is almost wholly protected by bone skeletal injuries were four times as frequent as internal ones.

Subjects generally showed surface markings of violence. However in a rare case superficial surface markings such as a scalp contusion was totally absent.

Although these subjects died from trauma and subsequent complications. The exact course, mechanism of death were not always clear cut. Irreversible shock, vital organ damage and uncontrolled haemorrhage were overlapping causes of death.

Acknowledgment

I am thankful to the Dean, Medical College Hospital, Aurangabad for his kind permission to publish this paper.

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A Study of Eosinophil Count in Allergic and Vasomotor Rhinitis

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A study of nasal smear eosinophils and peripheral blood eosinophils has been conducted in 37 cases which were divided into three groups - control, nasal allergy cases and vasomotor rhinitis cases. A significantly high eosinophil count has been observed in nasal smear and peripheral blood in cases of nasal allergy.

Introduction

Since the findings of eosinophils in nasal secretions by Bizzozero in 1887, the study of nasal smear eosinophils to diagnose cases of allergic rhinitis has become a standard procedure. When combined with a study of the eosinophils in peripheral blood, it gives a good indication about the presence or absence of an atopic process.

The present study was conducted to study the utility of these techniques in patients of allergic and vasomotor rhinitis.

Material and Methods

The cases were selected from the E. N. T. O. P. D. and were divided into three groups :—

1. **Control group** : Comprising ten, normal and healthy individuals without any known personal or family history of allergy. They belonged to the 23-42 years age group.

2. **Allergic Rhinitis Group** : Comprising 17 patients in the 16-40 years age group. This group included only those patients who gave a history of nasal obstruction, fits of sneezing, itching of the nose, eye and palate and nasal discharge on

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exposure to an allergen or strictly in a certain season. In addition to this, a positive family history of allergy, collarteral allergies like eczema and asthma, predisposing factors like cold, change in weather, exertion and excitement, occupational hazards and psychological factors were also sought for. Conjunctival injection and pallor and oedema of nasal mucosa were considered primary requisites together with a positive history, for the diagnosis of nasal allergy.

3. **Vasomotor Rhinitis Groups** : Ten cases of V. M. R. patients in the age group of 18-36 were included in this group. The examination findings in this group were similar to the allergic group, but the main differentiating features of VMR from perennial nasal allergy were the absence of any offending allergen and the absence of itching of nose and conjunctiva and presence of a watery nasal discharge.

A detailed history and thorough physical examination supplemented by complete ENT examination was done for allocation of the cases into the various groups. A nasal smear for eosinophilis and absolute eosinophil count was done to compare the cellular response in blood and nasal smears.

Nasal Smear for Eosinophils : Nasal discharge from each nostril was collected by asking the patient to blow from each nostril separately on cellulose paper strip. For those patients who were unable to produce enough nasal secretion, a sterile cotton swab was inserted along the floor of the nostril and left in situ for one minute and then removed. Finally, the secretions collected were transferred to clean glass slide for the preparation of thin smears.

Staining : Air dried smears of secretions were fixed for five minutes in absolute alcohol and then blotted and dried in air.

A freshly prepared mixture consisting of one part of Giemsa stain and 25 parts of distilled water was poured on the fixed smear and it was kept for 20 minutes. The stained smear was then washed in distilled water, blotted and dried in air.

The area of maximum concentration of eosinophils was selected for counting with a x 40 magnification oil immersion objective. In each case, one field was counted. If no eosinophils were found in the smear, the whole procedure was repeated. The smears were considered negative if the second examination failed to show any eosinophil.

Absolute Eosinophil Count : This was done in the usual standard procedure using a graduated mixing pipette, a counting chamber and eosinophil fluid for diluting the blood.

Observations

Nasal Smear Eosinophils : The nasal smear eosinophil examination was conducted in all 17 cases of nasal allergy but four patients failed to report for the second examination after the first negative smear. These four were, therefore, excluded from the study The mean eosinophil count per high power field was 10.92±0.62 in the 13 nasal allergy cases studied. Three cases of V.M R. failed to report for the second smear examination but the mean eosinophil count observed in the remainder was 7±1 54 and none in the control group showed any eosinophil in the nasal smear.

Absolute Eosinophil count : The results of absolute eosinophil count in all the three groups are shown in the Table.

Discussion

It has long been believed that a predominance of eosinophils in nasal smear is one of the characteristic features of nasal allergy (Eyermann 1927 ; Hansel, 1934 ; Vaughan and Black, 1954 ; and Murray and Anderson, 1969). In cases of V.M.R. occurence of nasal smear eosinophils is occasional (Solomon, 1967). In this study the high number of eosinophils obtained in V.M.R. group may not be conclusive because of the difficulty in differentiating the perennial nasal allergy and V.M.R. However, nasal smear eosinophil picture in the present study stands in good agreement with the early reports on cases of nasal allergy.

Absolute eosinophil count of blood was found to be 706±66 per cu. mm. in cases of nasal allergy and 275±67 per cu. mm. in V.M.R. subjects. The increased number of blood eosinophils in nasal allergy was of statistical significance compared to that of vasomotor rhinitis and controls (vide Table).

It is interesting to note that Lowell (1968) considers an eosinophil count higher than 350/cu. mm. as diagnostic of atopic condition.

It, therefore, appears from the present study that high eosinophil counts in nasal smears and peripheral blood are significantly found in nasal allergy cases, much less frequently encountered in V.M.R. cases and never in controls and this is in agreement with the earlier reports in literature.

Acknowledgments

We are grateful to the Director, M.A.M. College and Associated Irwin & G. B. Pant Hospitals, New Delhi for her kind permission to use hospital records.

Table. Age nasal smear eosinophils, absolute eosinophil count in blood and skin reaction of patients of nasal allergy and vasomotor rhinitis compared to that of control subjects along with results of significance of variations amongst the different group.

Characterisation	Nasal allergy (II)			Vasomotor Rhinitis (III)			Control			Significance of variations amongst
	n	x ± S.E. (x)	S.D.	n	x ± S.E. (x)	S.D.	n	x ± S.E. (x)	S.D.	II Vs I II Vs III III Vs I
Age	17	25.65±1.64	6.74	10	24.40±2.03	6.43	10	30.70±1.80	5.68	Not significant
Nasal smear eosinophils	13	10.92±0.62	2.14	7	7.00±1.54	3.78	10	0.00±0.00	0.00	II Vs III significant
Absolute eosinophils/ c. mm (Blood)	17	706± 66	273	10	275±67	211	10	55±23	72	Highly significant
Histamine wheel sq. mm.	17	127.3±3.8	10.1	5	122.4±9.1	20.4	5	120.0±8.5	19.1	Not significant

Abbreviations

n ≡ Number of cases x ≡ Mean SE (x) = Standard error of mean

S.D. = Standard deviation Not significant (p=0.05)

Significant (0.01 p 0.05) Highly significant (p 0.01).

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New Approaches in Medical Education

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Medical Education today is in ferment. Wholesale changes are in the offing in the field of undergraduate and post-graduate medical education in our country. It is desirable that the need for the change and the desirable changes in undergraduate medical education are examined critically in the light of the existing system and its products.

Our country is plagued with quantitative and qualitative deficiencies in medical manpower. It will take long time for our country to reach the norm of one doctor per thousand population. However, the ratio of one doctor per 3500 population recommended by the Health Survey and Planning Committee in 1961 as an immediate objective has almost been reached, taking into consideration the Fourth Plan target of 1, 37, 930 doctors by 1974 and the addition every year of about 12,000 doctors. Though this ratio is much lower than that prevailing in the advanced countries, it compares favourably with many of the less developed countries (Mead, 1970).

The glaring deficiency is in the distribution of doctors. Over two thirds of the total doctors are found in the urban areas and some twenty per cent of the doctors are in private practice (Institute of Applied Manpower Research, 1970), most of these being thought to be in urban areas. This imbalance in distribution is a qualitative problem also as it is due, in great extent, to the lack of orientation and skills in rural medical and health care on the part of the doctors.

The other problem is that of general standards of medical education. It is apprehended in certain quarters that there has been a gradual deterioration in this regard. Some of the recent events abroad have brought this question into the fore-front. However this problem and that of the imbalance in distribution of doctors are closely associated with the system of medical education and the methods adopted in training medical graduates. The rise in standards of medical education has to be for its own sake and for the nation's sake and not for the sake of exporting "good" doctors, who are trained at great cost to the nation, (Notes and News, 1970) to other countries. Those countries, of course, are at liberty to choose the type of doctors they want. If our own system of medical education prepares doctors for our own needs and not keeping in view the requirements of the General Medical Council of Great Britain or some such body, the problem of migration of doctors will disappear in due course.

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The Western medical education which we inherited remains more or less the same as it was at the time of independence. It was and is, in spite of certain half-hearted efforts to improve it, an education designed to cater to curative services in hospital setting with the help of costly modern equipment and complex laboratory services. As these conditions prevail in our cities only, doctors who are trained in such milieu naturally will have an urban bias. The lure of money also plays its part and the great majority of doctors in urban areas provide care mainly to the rich. The rich are able to pay the private practitioners for their services and are in positions of better access to Government Hospitals. In general the paying capacity of the rural folks is poor and the rural rich going to towns and cities for medical care, the doctors are reluctant to establish themselves in rural areas. The Government doctors posted to rural areas are faced with problems such as difficult living conditions, lack of accomodation and facilities for transport, communication and children's education and professional isolation. However important these reasons may be, the fundamental block remains the urban-oriented education coupled with elitist bias. These doctors are neither trained nor oriented adequately for the health work in rural areas, where four-fifths of our population live and whose needs are urgent. Many Government doctors are preoccupied with manoeuvres to get a transfer.

There has been an 'explosion of expectations' in the people as regards medical services and this along with the concept of 'welfare state' and the concern of our Government for 'growth with social justice' call for far-reaching changes in the medical teaching which has so far been a non-selective accumulation of knowledge built up over the years.

The above deficiencies are well recognised by our leaders and medical educators and many attempts have been made to remedy them. However at no time the need for total change in medical education was thought of, the changes attempted being only ad-hoc in nature and generally touching the fringes of the problem. A case in point is the establishment of departments of Preventive and Social Medicine and the great hopes placed on them is effecting the desired changes in orientation and skills of the medical graduates. These hopes were mostly belied. There have also been attempts to import ideas and programmes from abroad, without much thought as to their suitability to our environment, as exemplified by the clamour for 'medical assistants', 'barefoot doctors', **etc.** and sometimes total importation of syllabi and curricula framed by foreign agencies for their own purpose. It is worth noting that the products turned out by our National Institutes, which were established with national aims and ideals, are all migrating to the U. S. A. or U. K., finding themselves uneasy not only in rural India but in Indian cities also.

The new approach to medical education in the above contexts has to consider two main factors, **viz**, imparting the knowledge and skills necessary for delivering health care and developing the correct attitudes and orientation required for rural health work. The modern educational methods should be applied in medicine also and the teaching programmes must be shaped in terms of the aims to be achieved (Reddy, 1971; Bose, 1965).

The first important thing is to define the health needs of the country/community. Once this is done and the resources are listed a national health plan can be made, which describes the health tasks to be undertaken and the facilities to be provided. Medical educators have to define their objectives based on the tasks to be faced by the doctor in his community. All this means that medical education should be in line with the national health needs and not independent of them, because medicine is 'scientific in method, but social in purpose' (Ramalingaswami, 1973).

There is no need to improve upon the definition of the Basic Doctor as given by the Medical Education Committee. "He is one who is well conversant with the day to day health problems of the rural and urban communities and who is able to play an effective role in the curative and preventive aspects of the regional and the national health problems. Besides being fully well-up in clinical methods, **i e.**, history taking, physical examination, diagnosis and treatment of common conditions, he should have the competence to judge which cases are required to be referred to a hospital or a specialist. He should be able to give immediate life-saving aid in all acute emergencies. He should be capable of constant advancement in his knowledge by learning things for himself by having imbibed the proper spirit and having learned the proper techniques for this purpose during his medical course".

The idea is to have a primary or first contact physician who will be incharge of a defined community for extending comprehensive health care which includes curative, preventive and promotive services. The private practitioner in his capacity as famity doctor also is expected to deliver the above services to the families under his care, The community doctor in his area, which corresponds to the Primary

Health Centre area in the present set-up of our country, will have four main functions, **viz**, (1) provision of personal medical care for individuals and families, (2) making community diagnosis and instituting community action, (3) teaching and supervision of his team members, and (4) community leadership in health matters. These functions are reflected in the definition of 'Basic Doctor' above, which also lays stress on participation in the national health programmes and on continuing education of the doctor.

These functions demand certain abilities of the doctor. The objectives of the medical education should be to impart these abilities and at the same time produce the attitudes favourable for performing the functions. In other words education is nothing but production of changes in knowledge, attitudes and skills and the objectives should be in terms of changes in behaviour in thoughts (knowledge), interest (attitude) and actions (skills). Knowledge and attitude are prerequisites for performance of the skills. The entire process of selection of students, formulation of curriculum, teaching and training and assessment should revolve round the idea "What the graduate is expected to be able to do at the end of the course ?" (Guilbert, 1968).

I venture to cite some examples to illustrate the concept of educational process. The functions of the doctor enumerated are mainly concerned with generalities. It is essential to list the particular tasks (and objectives) under various activities or components of community health. Medical care, maternal and child care and family planning, communicable disease control, nutrition, environmental hygiene, health education and administration are the important activities of a health centre or with some variation of the family doctor. If we consider the infectious diseases, the knowledge, attitudes and skills required to tackle them are as follows :—

Knowledge : Knowledge regarding incidence and types ; diagnosis and treatment ; social and public health aspects ; care of contacts, rehabilitation, health education **etc.**

Skills : Methods of investigation, diagnosis and treatment ; history taking, clinical examination, methods of health education, follow-up of cases, record keeping **etc.**

Attitudes : Objectivity ; appreciation of need for not only medical care but rehabilitation, care of contacts and prevention of spread ; non-judgemental attitude (say with respect to sexually transmitted diseases).

To quote another example, for effective participation in the family planning programme the following are required (Mace **et al** 1974).

Knowledge : Why family planning (social, family and individual points of view) ; methods - acceptability, effectiveness and safety ; barriers in communication - socio-cultural factors, interpersonal relationships - and personal problems ; pregnancy termination - medical and legal aspects.

Skills : Individual interviewing and counselling ; group education, clinical techniques - diaphragm, IUCD, oral pills (examination), abortion, sterilization ; follow-up of cases, record keeping ; ability to discuss sexual matters in frank and unembarrassed way.

Attitudes : Personal acceptance of value of small family ; considering sex as an important and healthy aspect of life ; regarding cases as persons; unambiguous personal attitudes to contraceptive methods.

In like fashion, the other tasks faced by the doctor form the basis for educational objectives and the curriculum has to be designed to achieve these behavioural objectives. The traditional method of planning a course by a meeting of the board of Professors who prepare a list of subject contents in which process the existing course is merely modified with some reallocation of hours has to give away to the scientific methods of curriculum design and assessment based on modern educational practices.

Attention has also to be paid to equip the doctor with the self-learning techniques so that he can continue his education beyond the walls of the institution. He should be sufficiently oriented to employ the scientific method whenever feasible and draw conclusions and improve his knowledge and skills. "If you give a man a fish, he will feed himself once. If you teach him to fish, he will feed himself all his life".

Selection of students for medical course : The present systems tend to favour the urban elite with better command over English language and with a degree of personal refinement. Though in foreseeable future English will be the medium of instruction the excessive emphasis on English language is uncalled for and also the subtle bias towards urban-educated students in interviews and other forms of personal assessment needs to be avoided. Instances of unfair preferences being shown to children of officials and influential persons are not unknown. All the above perpetuate a distinct disadvantage to students from the ordinary sections of the society especially from rural areas. Either 'real' tests for intelligence and aptitute have to be devised or admissions be based solely on performance in relevant science subjects in the qualifying examination. The accepted schooling formula of 10+2 years should continue to be the requirement for admission.

Duration of the course : The duration of the medical course and the different phases therein should be governed not by tradition or any other arbitrary decisions, but solely by the educational objectives laid down for the course. Here it may be pointed out that the basic sciences have to be cut to the required size without stressing the minutiae. The stress should be on the applied aspects which are useful in future practice. It is commonly observed that each professor and his staff presume that the student is studying their subject only and are more interested in saturating his brain with facts than in trying to synthesize their subject with others keeping the total health of the total man in view. This criticism also applies to some teachers of clinical disciplines as well.

Teachers : It need not be emphasized that adequate teacher: student ratio is a must for good education and this can be achieved either by employing more teachers or by reducing the admissions in present medical colleges. In the event of the latter procedure, more colleges have to be opened to achieve the desired doctor : population ratio. Increase in number of medical institutions is also desirable from the point of view of provision of better medical facilities in unserved areas.

At present medical teachers are qualified in their respective specialities but are not generally trained in teaching methods. It is doubtful whether this training can be given to them under the existing circumstances, though it is highly desirable. Meanwhile teaching aids like audiovisuals have to be made use of to partly compensate for the above deficiency. Teaching aids at low cost have to be produced and distributed.

However the most important requirement from the teacher is his commitment to social objectives. The teacher is the 'change agent' in the preparation of tomorrow's physicians who in turn are going to be agents of social change. Therefore this aspect of selection of teachers has to be given due importance. However qualified a teacher might be unless he is committed to the social purpose of medicine his trainees will fail to deliver the goods to the community and the nation.

Assessment : Traditional examinations must give way to assessment methods which are designed to evaluate the student in terms of the educational objectives, i. e., whether he has succeeded in acquiring the necessary knowledge, attitudes and skills and whether his response to a given situation is appropriate.

The general guidelines for designing the undergraduate educational programme have been outlined above. The detailed schemes and the educational objectives sought to be attained have to be formulated by medical educators keeping in mind the needs and resources of the community.

Community - Orientation : As regards the specific problem of giving community-orientation particularly of rural communities, certain principles are presented below.

The educational system should be patient-oriented than disease-oriented. This means that the focus of attention should be total man in his total environment. The family, social and economic factors should be considered in diagnosing and treating the patient. The clinico-social case studies employing the methods of social work are useful in training the physician in this respect. The physician should also learn to guide his patients to the appropriate social welfare and public health services in the light of their economic considerations.

The community itself should be used as a practical laboratory and teaching medium to give the necessary orientation. It is said "community is the ward and each household a bed". The urban and rural field practice areas attached to medical colleges have been functioning for this purpose but their success has not been complete and uniform. More facilities and better discipline and motivation on the part of the staff and students are required to make full use of these field practice areas. In these health centres model health services are provided to public and the students learn by observation as well as participation. The undergraduate students should be trained in the rural field practice area through family study programmes by which they can study the family in relation to health and disease and also the natural history of disease. They can also study the growth and development of children in families which gives them the necessary insight into child life and health in rural areas. Students should conduct, as short-term projects, and participate in, programmes intended to assess the health needs of rural communities and to measure the effectiveness of the services provided. Experience in such surveys helps the students to draw conclusions on their own training requirements. Students in pre-registration phase should be involved more actively in community diagnosis, health care delivery and national health programmes and should learn how to elicit and obtain villagers' cooperation and practice of medicine under rural or other difficult conditions where modern equipment and laboratory services may not be available. Specifically the concepts to be ingrained are team approach, continuous and comprehensive care, community involvement, administration of health centres, health education and survey methods (Robinson, 1973).

The teaching of medical students by selected health centre doctors and privat practitioners is being contemplated and this method is welcome as it exposes the students to special problems encountered in practice and their solutions. Unde the present conditions a raw graduate posted to a health centre or a doctor setting up practice is faced with some unexpected problems which the earlier training might not have prepared him to face. For example, as regards the intricacies of administration, he is a novice and is open to exploitation. Hence training under a basic doctor will enable him to know the duties of various staff and how to get the team going.

Participation in voluntary services during student career should be encouraged. Campaigns under the auspices of organisations like the National Service Scheme will help the students to acquire first hand experience of problems in rural areas and to learn how to approach the community and solve some of their problems.

A group of sciences which are neglected and which are as basic to medical science as are Anatomy, Physiology and Biochemistry are the Behavioural Sciences. The relation between human behaviour and health has to be appreciated by the student and the relevant socio-cultural practices, habits and customs to be considered either in individual treatment or in community health work. The training in behavioural sciences will help the doctor in appreciating what illness means to patient in terms of social disruption and psychological upset. More than this the doctor should overcome the communication barriers between himself and the patient. It often happens that the language used by the patient coming from a different, usually lower, social class fails to convey the full significance to the doctor. Hence he has to adapt so his patient as he has more felicity in this respect. Most of our patients are passive in accepting the doctor's advice and actions and some of them are apprehensive also. It is the doctor's duty to be courteous and sympathetic and to study the patient in toto and allay the fears and reassure him. He should impress on the patients the need for treatment especially in case of chronic diseases.

An elementary study of economics and politics should be part of the curriculum. Economic and political factors deeply influence health and health care delivery. The national aspirations, constitutional provisions, society's responsibility and concern of Government towards people's health and productivity are to be stressed.

A few general principles which strike to me as important are outlined above and their applicability and mode of application are left to the medical educators who are once again busy reviewing what is on hand and planning new changes. We hope the day is not far off when we can greet our social physicians.

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Interaction of Child Health with Community Medicine*

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Community medicine as a concept extends much beyond the narrow confines of 'public health', 'social and preventive medicine' or 'general practice in a rural setting with limited or poor resources'. It is all this and much more.

Appropriately, the term community medicine should include all concerns and activities which aim at providing comprehensive health care to every individual in the community. In essence it is good medical practice.

Clinician treated the patients who are sick, in pain or incapacitated and who sought his help. Traditional medical ethics demanded that he did not solicit patients and therefore he was essentially inward looking and he confined himself to an ivory tower around him. On the other hand, the public health official developed programmes directed to the entire community and provided its collective health needs, **viz.** environmental sanitation, malaria or small pox eradication programmes **etc**. Both the groups of health functionaries did admirably well in their own respective domains. It was however soon recognised that in every population, there exist groups of people who are not so sick that they must go to the hospital or seek medical advice, but who nevertheless are very vulnerable. They are at high risk to develop disease or irreversible handicap if proper medical attention is not given at the appropriate time. A pregnant mother may not seek medical help but it is essential to examine her antenatally to identify complications of pregnancy as toxemia or foetal position. Lack of good obstetric services may cause maternal or foetal death or permanent arrest in the development of the newborn.

A moderately malnourished child may not be recognised at risk by the family and medical attention may not be sought. Very high mortality in preschool children

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**Professor and Head

in India directly due to malnutrition or increased severity of infection in association with malnutrition can easily be prevented if these children are identified and appropriate health measures adopted contacts of patients with tuberculosis or leprosy are other high risk groups which need help.

In this concept of clinical medicine, both the clinician and the public health official should concern with the health care of this group besides their conventional roles. This group is the overlapping area in the venn diagram of health services.

In this approach to community medicine clinician albeit pediatrician has a major role in both teaching and practice of community medicine. Pediatrics is the clinical area which provides the ideal medium for demonstration of application of these principles. The pediatrician is concerned with promotion of optimal growth and development of children. He identifies factors that retard or arrest growth of the child and mitigates their effect by prevention and adequate treatment.

There is, thus, a considerable overlap in the academic and service programmes of Pediatrics and Preventive and Social Medicine. This makes them ideal partners not competitors in the practice of Community Medicine. Thus Community Medicine should not be considered a separate career or discipline for trainees in Preventive Social Medicine only. This should be a part of all clinical training. Community Medicine should therefore, be not just the old wine in new bottles or a new name for Hygiene and Public Health or Preventive and Social Medicine. It should be a dynamic concept. Thus educational and service programmes relating to child health for trainees in community medicine should be adapted to meet the desired learning objectives. In programmes and activities of Community Pediatrics are usually not spectacular and dramatic. These lack luster and therefore should receive greater prestige and financial support from health administrators.

In this approach, the child health forms the core of postgraduate educational programme in community medicine. Some of the desired goals and learning objectives in the field of child health for postgraduate trainees in community medicine are given below.

Goals

The community physician should be able to monitor growth and develop ment of children and intervene whenever the child's physical, intellectual and social development appears to be in jeopardy. He should be able to identify factors which promote health of the child and causes which obstruct operation of these factors. He should be able to manage common health problems of children especially those which if detected and managed early prevent irreversible handicap. He should be capable of influencing decision making bodies in the country for providing support for health and welfare services.

Learning objectives :

1. Helps the children achieve their optimal growth potential.
    - (a) Recalls the mean anthropometric measurements and behavioural development of children at different ages.
    - (b) Demonstrates correct method of using instruments for assessing growth and development of children.
    - (c) Assesses the growth of a child at every clinical encounter and recognises early the delay or arrest in his growth by comparing it with the growth norms in the community.
    - (d) Identifies social and biological factors responsible for slow growth of the child.
    - (e) Undertakes appropriate activities to promote growth of the child (health education, dietary advice, supplementary feeds, preventive immunisation, referral to appropriate agency).
2. Diagnoses and treats common illnesses in children, in the local geographic area, prevents their recurrence and rehabilitates the patients with chronic illnesses in the community.
3. Recognises common pediatric emergencies and manages them adequately or provides first aid before referral to the appropriate agency.
4. Distinguishes newborn babies requiring special care from healthy newborn babies and provides appropriate treatment to prevent disease or irreversible handicap.
5. Recognises the behavioural disturbances in children, identifies the social factors responsible for maladjustment and refers these to appropriate agencies for management.
6. Prescribes appropriate immunisation schedule for a child at the first clinical encounter and when necessary at subsequent visits.
7. Recognises the side effects of immunising agents and takes appropriate measures to mitigate these.

8. Informs the parents about the quantity and quality of cheap, locally available and culturally acceptable foods necessary for the normal health and growth of the child.
9. Recognises the nutritional deficiency syndrome and assesses their severity.
10. Advises the parents about the dietary management of the malnourished children within their financial means and when necessary seek help from appropriate welfare agencies for supplementary feeds for the child.
11. Recognises the possibility of genetic disorders in congenital or familial illnesses and counsels the parents on the probability of transmission of the defect to the offspring and desirability of preventing birth of such babies. Offers premarital counselling to couples with history of developmental disorder in the family of one or both of the parents.
12. Identifies child health problems of national importance.

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Abstracts

Abstracts of the papers presented at the 12th meeting of the North Chapter of the Indian Academy of Medical Sciences held at Rohtak on 25.4 76

House Physicianship - An Appraisal

C. Prakash and R. R. Gupta

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The objective of a house-physician is to learn the art of diagnosis and management of patients. Inspite of the period being most vital in the development of a good clinician and also its socio-economic value no curriculum has been laid down, to attain this ojective. Present study was carried out to find out the requirement of a house physician and also to evaluate in attaining the objective. A detailed questionary was framed enquiring the facilities of learning, the art of diagnosis and management, work load and suggestions regarding modification in the curriculum of house job. In all 45 house-physicians who had completed one year house job in medicine/allied specialities participated in this study. They were divided into three groups :-Group A (25) who had completed one year house-job in medicine; Group B (15) who had completed one year house-job in Paediatrics/Psychiatry/Skin & VD/ Tuberculosis/Radiology; Group C (5) : 6 months in Medicine and 6 months in other speciality. About 70-80 per cent of the house physicians feel competent in the medical diagnosis and management in their speciality after one year house job, but majority of them i.e. more than 70 per cent feel necessity for further training in other allied specialities. It was an unanimous decision that the house job is essential for training but suggested certain modifications i.e. during one year house job, they should be posted in other specialities also.

Life Threatening Complications of Enteric Fever—A Current Reappraisal

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All patients coming to Medical College and Hospital, Rohtak between Ist May, 19 4 to 30th September, 1975 were screened for enteric fever and 125 consecutive culture positive (blood/urine/stools) cases of enteric fever were studied. A meticulous daily observation of clinical features and progress of the patient was kept in order to record the complications observed during the period of illness.

Out of a large number of complications mentioned in the literature and observed herein, gut perforation, gut haemorrhage, encephalopathy, myocarditis and toxaemia with circulatory failure were serious enough to be labelled as "life threatening" and were responsible for 10 deaths occurring in this series. The pattern of these complications appeared to be somewhat different from the one reported in literature in the past and needed revision. A current reappraisal of these complications shall be presented.

Long Standing Post Burn Contractures—Secondary Effects they Produce on Deeper Structures and their Management

C. P. Sawhney

P. G. I., Chandigarh

The paper stresses the importance of contracture of normal skin surrounding a contracted scar which also requires to be released. Incisions at right angle to tension lines are most effective. Commonly, deeper structures e.g. fascia, blood vessels, nerves, muscles and capsular ligaments are also shortened. Facial contractures require multiple incisions, collateral ligaments across meta-carpophalangeal joints require division, but other contracted tissues require gradual stretching by static/dynamic splints in post operative period. Accompanying sub-luxation/dislocation of small joints of hands and feet may need surgical correction or traction splints. In infancy and childhood demineralization of bones and dysuse atrophy of affected muscles is not uncommon. They get corrected after return of function. The accompanying growth abnormalities are difficult to manage. Consequently early management to prevent them is recommended. The author outlines following principles in management of contractures e.g.

(1) Release contracting scar and adjoining contracted skin;

(2) Resurfacing with skin grafts;

(3) Maintenance of correced position for three weeks by splints;

(4) Prevention of skin graft contraction by wearing splints for six months; and

(5) Active physiotherapy.

Thyroid Lymphography

T. V. Babu Singh, R. K. Keswani and A. L. Jain

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This is a technique of visualising thyroid gland and assessing its anatomical configuration and various disorders. 1.5 ml. of ultra fluid lipiodol is injected in each lobe of thyroid without anaesthesia. The rich lymphatic network takes up the contrast medium and produces a lymphogram. Subsequently within 2-24 hours, the contrast medium flows into the regional lymph nodes and these are also visualised in their normal or pathological states. Rapid outflow of the medium indicates increased lymphatic flow and thus hyperfunctioning of thyroid gland. The study in Department of Surgery-II comprised 36 thyroid lymphograms and following types of information, correlated with various functional and pathological states was obtained.

1. Normal reticular pattern representing normal thyroid lymphogram.
2. Size of thyroid gland e.g. increased size was seen in puberty goitre and colloid goitre.
3. Retrosternal extension.
4. Filling defects representing single nodules.
5. Fluid levels in cystic cavities of thyroid.
6. Puddling of contrast medium was seen in carcinoma.
7. Rapid clearance of contrast medium was seen in thyrotoxicosis.
8. Multinodular goitre produces a stormy, cloud appearance with absence of normal reticular pattern and definite filing defects.
9. Finally cervical lymphnodes were visualised when there was no blockage of cervical lymphatic vessels.

The Mechanism of Hypoferaemia in Acute Infection

Ramesh Kumar

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Fall in serum iron levels has been reported to occur consistently in acute as well as in chronic infections. This hypoferraemia is believed to result from abnormal trapping by the reticulo-endothelial cells of the endogenous iron released from senescent red cells. Studies of the storage iron in acute and chronic infections (from both biopsy and autopsy material) and studies of the pattern of hypoferraemia in acute and chronic infections, performed presently show that the mechanism responsible for hypoferraemia in acute infections is not quite the same as for the hypoferraemia of chronic infections. Unlike in chronic infections, hypoferraemia of acute infections is not accompanied by increase in storage iron, nor is it accompanied by hypotransferrinaemia. Significant hypoferraemia is also noted in aseptic inflammations, although to a lesser degree. A new hypothesis is presented for the mechanism of hypoferraemia of acute infections suggesting that it is due to a dual effect of (a) adrenocorticoid stimulation of general stress effect and (b) direct utilisation of iron by the microbes responsible for infection.

Allergic Broncho-Pulmonary Aspergillosis

S. K. Malik, G. K. Khattri and P. Talwar

P. G. I., Chandigarh

Pulmonary disease secondary to invasion by the spores of aspergillum is frequent in patients of chronic lung disease, in particular tuberculosis and other conditions of depressed immune state. However, the allergic form of pulmonary aspergillosis where immune mechanism are involved is recognised only infrequently. We recently had the opportunity to confirm the diagnosis of allergic broncho-pulmonary aspergillosis in five patients. The striking clinical features were signs and symptoms of bronchial asthma (5 cases), recurrent chest infection (2 cases), incidental hemoptysis (2 cases), eosinophilia in the blood and pulmonary secretions in all cases. In 3 there was history of expectoration of dark brown material from the lungs. Skiagrams of the chest showed recurrent segmental consolidations in 4 and 'glove finger' appearance in 2 cases. The immediate Type I and delayed Type III cutaneous reactions to specific antigen as well as the precipitating antibody were found positive in all except one patient who was not tested. Two patients had severe symptoms which cleared with steroid therapy. A variable degree of damage in the form of residual pulmonary fibrosis or bronchiectasis remained in all the five cases under discussion. In conclusion this diagnosis should always be suspected in patients with recurrent pulmonary infections of nontubercular origin, particularly in those where the simple causes of pulmonary disease with eosinophilia have been excluded.

T and B Cells in Rhesus Monkeys

N. K. Ganguly

P.G I., Chandigarh

T and B cells were determined in 30 rhesus monkeys and 17 normal human beings. T cells were determined by rosetting and B cells by rosetting using human C'3 and immunofluorescence method. It was observed that T cell range was similar in both and B cell percentage was slightly higher in monkeys Monkey B cells had immunoglobulin receptors for IgG, IgM, IgA total of which corresponded with total B cell rosetted. Serial sampling in six monkeys for six weeks showed no difference within the monkey but variation from one monkey to another was obtained.

Epedemiology of Hepatitis Type B in and around Chandigarh, Northern India.

S. R. Pal, S. Choudhury, D. V. Datta, and P. N. Chhuttani

P.G.I., Chandigarh

Serum samples from 460 sporadic acute hepatitis cases collected during the period March, 1972-February, 1976, were tested for HBsAg by discontinuous counter immunoelectrophoresis. The cases with definite history of parenteral infection were excluded from the series. Eighty-four out of a total 460 patients were positive for HBsAg. Since the number of positive serum samples per month in different years was small, the results of different months were pooled individually. A significantly high proportion of HBsAg positive hepatitis cases was noticed in the months of July (12 per cent), August (18 per cent) and September (16 per cent). The supposed month of infection with hepatitis B Virus (HBV) was considered to be three months earlier than the disease month. No significant correlation was found between the proportion of positive cases in the disease month and the mosquito density, rainfall or temperature at the supposed month of infection. The maximum mosquito density was noticed in the months of August and September during and after the tropical rainy season (June, July and August). The hot summer months were April, May and June and during this period peak incidence of gastroenteritis was noted being 12 per cent, 17 per cent and 13 per cent respectively. A direct linear relationship could be established between the proportion of HBsAg positive hepatitis cases in the month of infection with HBV. It is suggested that the maximum rate of infection with HBV occurred in the months of April, May and June, a period when gastro-enteritis is common.

Abstracts of the papers presented at the 13th meeting of the North Chapter of the Indian Academy of Medical Sciences held in the P.G.I., Chandigarh on 21.11.1976.

Ventilatory Capacity of Healthy Adults

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This study was carried out in two phases. In the first part ventilatory capacity of 790 males, all non-smokers and with different backgrounds, was assessed by means of the measurement Peak Expiratory Flow Rate (PEFR). Low values of PEFR were observed in the rural residents. PEFRs in the better income class were only marginally higher than the low income group. Separate observation made in 100 cigarette smokers showed a distinct disadvantage for the heavy smokers.

The second set of observations were made in 180 healthy college teachers belonging to the city of Chandigarh. The mean values of PEFR were : males, age 37.5± 7, Ht 169 ± 6.6 PEFR 524± 66.5, L/min; females, age 34.65± 7.35, Ht 156.7± 5.2 PEFR 385± 42.5 L/min. These measurements were slightly better than those observed earlier in healthy adults. The mean PEFR of 89 age and Ht matched male farmers was 477± 59.0; difference from the teachers was significant ($P<0.001$). Similarly the PEFRs for 185 apparently healthy house wives from the city of Chandigarh were lower than the corresponding values recorded for the female teachers. The relevance of these findings and the role of different background variables affecting ventilatory capacity of adults will be discussed.

Non-tubercular Spinal Abscess

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Department of Neurosurgery, Postgraduate Institute of Medical Education and Research, Chandigarh.

Non-tubercular spinal abscess is rare but potentially curable lesion if detected early and operated upon before the complete loss of function occurs.

During the last 11 years we came across 22 cases of non-tubercular spinal abscesses in 21 patients, out of which 16 were males and 5 females. Most of the cases occurred in 2nd, 3rd and 5th decade but no age group was immune. Fourteen were located in the epidural space, 6 were intramedullary, one was subdural and one was epidural along with intramedullary. All the patients had sensory and motor deficit and 19 patients had bladder involvement as were at the time of admission. Plain X-ray spine showed destruction of pedicle in one patient, osteomyelitis in one patient and it was normal in 20 patients. Myelogram revealed complete block in 18 cases, incomplete block in 3 patients and in one it was not done. Fifteen abscesses were located in the dorsal region, 5 in lumbar region, one in cervical region and in one unoperated case extent could not be known. Twenty one cases were operated.

Source of abscess could be traced in 5 patients, infection having occurred from stab injury to the spine in one patient, skin infection in one, meningitis in one and osteomyelitis of vertebra in one patient. Staph. pyogenes was grown in 16 patients, E. Coli in one patient and pus was sterile in 4 intramedullary cases.

Fourteen patients improved, 4 remained unchanged, one patient deteriorated and three patients died giving a mortality of 13.6 percent.

Spina Bifida Occulta

Hardas Singh Sandhu

Medical College, Amritsar

Seventy-five cases of spina bifida occulta were treated during the period 1965-1976. There were 43 female and thirty-two male patients. They were from 2 years to 26 years of age, 68 patients were between to 15 years of age. The presenting symptoms were muscular weakness, of lower limbs, with or without sensory impairment. Loss of bladder control was present in 29 cases. Anal sphinctor was involved in 11 cases with deformity of feet in 7 cases. Trophic ulcers were present in 9 cases. X-ray picture showed defect of one vertebra in 11 cases, in others two or more vertebrae were affected. Myelography revealed diastemotomylia in 4 cases. Dermoid cyst in 2 cases. At exploration there was fibrous constriction of dural tube in 21 cases, abnormal fibrofatty mass in 22 cases.

Diastematomyelia in 5 cases, dermoid cyst in 3, bony bridge lying in coronal plane in 2 cases, spinal cord going into fibrofatty mass outside the vertebral canal in 6 cases. Forty-two cases showed definite improvement. There were 7 cases who showed doubtful improvement, while in 21 cases there was no improvement. There was temporary increase in neurological deficit in one case. One patient died of convulsions on the 7th post operative day.

Rheumatic Heart Disease - an Autopsy Study of 260 Cases

B. N. Datta and Bharti Nagrani

Department of Pathology, Postgraduate Institute of Medical Education and Research, Chandigarh

This department has encountered 260 cases of rheumatic heart disease among 4300 autopsies over a period of 12 years between 1964 and 1976. There are 2.2 males for every female with an average age of 26 years. Mitral Valve alone is involved in 37 per cent, mitral and aortic in 27 per cent, mitral, aortic and tricuspid in 23 per cent. Thirty-seven per cent cases show organic tricuspid valvulitis. A figure far higher than Western countries (10—12 per cent). Acute rheumatic carditis was rare at autopsy, active Aschoff bodies were found in 26 per cent cases, pericarditis in 49 per cent and 13 per cent cases were complicated by bacterial endocarditis.

RHD is the commonest fatal cardiac disease.

Long Term Effects of Fluoride Administration - An Experimental Study

S. S. Makhani, S. P. Thapar and Parminder Singh

Medical College, Patiala

Histological pattern of the human osteofluorosis is varigated in appearance ranging from complete destruction of bony architecture, immature bone to a mature normal bone with normal Haversian systems. In experimental series, the bones of the rabbits exhibit non-mineralization of osteoid tissue associated with destruction of bone. In some cases patterns stimulating the paget's disease and hyperthyroidism are seen. Radiologically the bones show the appearance of osteoprosis which may result in pathological fracture. Addition of phosphates make the bones sclerosed. Addition of phosphates and magnesium carbonate make the bones brown. The ossification of interosseous membrane as a parameter of detecting the earlier manifestation of fluorosis is not tangible as it has been observed even in the control series. Electrophoretic pattern of serum proteins is deranged. There is fall in albumin and rise in gamma globulin. Levels of acid phosphatase and succinic dehydrogenase enzymes are depressed. Degenerative changes in liver and kidney are seen. Parathyroids are hypertrophied.

Comparative Study of Upper Gastrointestinal Endoscopy and Radiology in Peptic Ulcer

S. R. Naik, M. K. Arora, V. P. Sharma and S. K. Mehta

P. G. I., Chandigarh

Sixty-nine patients who were diagnosed clinically to be suffering from peptic ulcer were selected randomly to compare their barium meal studies and endoscopic findings (using ACMI, Forward viewing panendoscope). Two radiologists independently reported on the barium meal studies of these patients without any knowledge of clinical or endoscopic findings. The radiological criteria included for the diagnosis of peptic ulcer were ulcer crater, scarred and deformed cap and pseudodiverticulum. Irritable or spastic duodenal bulbs were analysed separately.

It was observed that in 27 patients (39.13 per cent) duodenal ulcer was established both by endoscopic and barium meal examination. In 32 patients (46.38 per cent) no ulcer could be detected both by endoscopic and barium meal examination. In 7 patients (10.14 per cent) ulcer was diagnosed on barium meal examination, but could not be confirmed on endoscopic examination. In 3 patients (4.35 per cent) endoscopy revealed ulcer but barium meal was normal.

So there was a good correlation in 85.51 per cent of the patients.

One out of 5 patients reported to be having irritable or spastic duodenal bulb radiologically had duodenal ulcer on endoscopic examination.

Cord Blood Porphyrins - A Quantitative Assay in 30 Newborn Babies

F. Handa

Department of Skin & V. D., Govt. Medical College, Patiala

A quantitative assay of free erythrocyte porphyrins was done in umbilical cord blood of 30 newborn babies by spectrophotometric method. Free erythrocyte protoporphyrin (EPP) was found to be 74.58 ug./100 ml. packed erythrocytes (ug. per cent) and free erythrocyte coproporphyrin (ECP) 0.77 ug./100 ml. packed erythrocytes (ug. per cent) with a standard deviation (SD) of ±29.99 and ±1.48 ug. per cent respectively. Co-relation of EPP and ECP with sex and body weight of the newborn was found to be statistically significant.

Evolution, Resolution and early Diagnosis of Optic Disc Oedema

M. M. Singh Hayreh

Department of Ophthalmology Medical College, Patiala

Early diagnosis of ODE (optic disc oedema) in raised intracranial pressure is of tremendous significance. Fluorescein fundus angiography has proved to be of considerable help in its diagnosis but its role in early stage has not been established. This study was carried out in 32 healthy rhesus monkeys by producing experimental progressive increasing intracranial pressure. The fundus examination was done by routine ophthalmoscopy; colour streoscopic funds photography, and flurescein fundus angiography during normal as control and serially thereafter.

During evolution of ODE it was found that swelling of optic disc (caused by swelling of the axons due to axoplasmic flow stasis), is the first change. Vascular changes like hyperomia are secondary in nature. The order of swelling was usually first lower than upper than nasal and temporal was last. Fluorescein changes appeared at later stage. The resolution of ODE followed the reverse suit. Stereoscopic colour fundus photography or other steroscopic method of optic disc examinations are the most sensitive means of detecting early ODE Routine ophthalmoscopy seems to be the least reliable in early stage. Angrography was useful in its diagnosis at a later stage. Normal angiography during the incipient stage does not rule out the presence of ODE. Effect of partial optic atrophy was also studied.

Epidemiology of Hypertension-based on Total Community Survey in the Rural Population of Haryana

S. P. Gupta, S. B. Siwach and V. K. Moda

Medical College, Rohtak

A total population survey to find out the prevalence of hypertension in the rural community of Haryana was conducted. One thousand one hundred and fifty-four men and 891 women comprising more than 95 per cent of the total eligible population were studied. The criteria for the diagnosis of hypertension were same as laid down by W.H.O. The prevalence rate of hypertension was found be most frequent in the upper socio-economic group and least in the lower socio-economic group ($P \angle 0.05$). It also had a direct correlation with the body built.

With increase in age the mean systolic and diastolic pressures showed a significant rise. A close correlation was also observed between the mean blood pressure and the body weight.

The results of the present study have been compared with other studies from India as well as abroad. Our prevalence rates are higher in comparison to other Indian surveys, but they are much lower as compared to studies from abroad. The possible explanations for these differences have been discussed.

Evaluation of Histological and Bacteriological Examination in Diagnosis of Osteo-articular Tuberculosis

Sat Vir Gupta, D. R. Arora, P. S. Maini and T. D. Chugh

Medical College, Rohtak

Sixty cases of osteo-articular tuberculosis diagnosed clinically and radiologically were investigated for bacteriological and histological diagnosis. The former included direct smears, concentration smears after hemogenisation stained with Z.N. and Auramine O for fluorescence microscopy. Cultures were made on L.J. and incubated for 6 weeks at various temperatures and in dark and light both. Various biochemical reactions and animal pathogenicity tests were done.

Histology was positive in 38 smears in 40 and cultures in 19 cases. Two strains were M. Kansassi. All were sensitive to streptomycin, PAS, Isonex, Ethambutol and Thicocetazone except one strain of M. Kansassi which was resistant to Isonex, the resistance Ratio being 16.

Effect of Drugs on Haemorrhage induced release of ADH in Rabbits

H. Datta, R. Roychaudury and P. L. Sharma

Department of Pharmacology, P. G. I., Chandigarh

Nicotine is a known potent stimulus, which can cause release of both oxytocin and antidiuretic hormone (ADH). Haemorrhage has been reported to cause selective release of ADH.

In the present study haemorrhage was produced in the anaesthetised rabbits by bleeding from the animal's carotid artery to the tune of 1/3 or the total blood volume over a short period. ADH levels were estimated before and 15 minutes after the haemorrhage. The estimations were carried out in ethanol hydrated rats as described by Jeffers, Levezy and Austin (1942). In a second set of experiments, effect of prior administration of drugs on the release of ADH was studied. It was observed that chlorpromazine, pheniramine maleate, and propyl alcohol blocked the release of ADH.

The possible implications of these agents in the management of clinical haemorrhage shock would be discussed.

Potentiation by Deoxysolalol of Prostaglandin-evoked contractions in Isolated Uterine Smooth Muscle : Specificity, Selectivity and Possible Mechanism of action

K. A. Narendranath, K. Rajkumar and P. L. Sharma

Deparment of Pharmacology, P. G. I., Chandigarh

In earlier studies from our laboratory (+) INPEA (N-isoproply-para-nitro) phenylethanolamine) and (+) sotalol has been shown to potentiate the prostaglandins evoked contractions of isolated rat and guinea-pig uterus The (—) INPEA and (—) sotalol had no such action, indicating that beta hydroxyl group may be responposible for steric hindrance. To test this possibility experiments were performed with deoxysotalol which does not have any beta-hydroxyl group in the side chain. The effect of deoxysotalol on contractions evoked by $PGF_2\alpha$ and 15-methyl $PGF_2\alpha$ in the isolated non-pregnant rat and rabbit uteri, and in pregnant rat and human uterine strips was studied. The specificity of action was tested studying its effect on the contractions evoked by other agonists like oxytocin, 5-HT, vasopressin, angiotensin and bradykinin. The selectivity of action was tested by studying its effect on prostaglandins evoked contractions of isolated fundus strip of rat, isolated tracheal chain and ileum of the guinea-pig and the fallopian tube of rabbit.

Deoxysotalol (100—300 μg/ml) per se had a marked stimulant action of the uterus. In smaller concentration (10 μg/ml) it had no appreciable effect on uterus but markedly potentiated the contraction evoked by prostaglandins. Also, the maximal response evoked by prostaglandins was increased. The potentiation was more marked with 15-methyl $PGF_2\alpha$ than $PGF_2\alpha$. The potentiation was both specific and selective, since deoxysotalol did not significantly affect the uterine contractions evoked by other agonists except oxytocin and the prostaglandins evoked contraction in other smooth musch preparations. Deoxysotalol may have a therapeutic potential if its selective potentiating action is confirmed in 'invivo' studies in animals and in women undergoing therapeutic abortion. The combined use of deoxysotalol and prostaglandin may require a smaller dose of prostaglandins and thereby result in a marked reduction in their severe systematic side-effects. Further work is in progress.

Plasma Cystine Aminopeptidase, Human Placental Lactogen and Heat Stable alkaline Phosphatase as indices of Placental Function —A Comparative Study

S. Jayaraman, S. C. Sikka, K. Dhall, G. K. Rastogi, K. S. Raghavan, A. N. Gupta and V. S. Mathur

Deparments of Pharmacology, Endocrinology and Obst & Gyanae.,
P. G. I., Chandigarh

One of the main problems in obstetrics is to confirm the clinical suspicion of placental insufficiency. The present study is a comparison of three tests of placental function namely cystine aminopeptidase (CAP), human placental lactogen (HPL) and heat stable alkaline phosphatase (HASP). The normal values of CAP, HPL and HSAP were established in our population by estimating these in 152 subjects who had normal foetal outcome. From these values normal curves with ± 1 and ± 2 S. D. were drawn.

Single estimation of CAP, HPL and HSAP were done in a mixed group of normal and complicated pregnancy (113 subjects). They received obstetrical care in our hospital. The infants apgar score at 1 minute and birth weight were correlated with plasma CAP, HPL and HSAP values. Plasma CAP proved to be the best in predicting foetal outcome ($X^2=36.27$; $p < 0.01$) followed by HPL ($X^2=8\ 06$; $p < 0.01$) while HSAP was of no value in predicting outcome.

Abstract of talk given by Dr. David A. Pyke at New Delhi on 4th November 1976 under the auspices of the Academy.

Genetics and the Aetiology of Diabetes : Studies in Identical Twins

D. A. Pyke

Diabetic Department, King's College Hospital, London

Previously diabetes has been thought to be due to a single recessive gene. This theory is based on the work of Pincus and White 40 years ago. It is now untenable largely because of studies in the offspring of conjugal diabetic pairs (both mother and father diabetic) among whom only 5 per cent are themselves diabetic.

We have carried out studies in identical twins and have now collected 125 pairs one or both of whom has diabetes. There are inevitable biases in the ascertainment of these pairs in favour of concordant pairs which, having two diabetics, have twice as much chance of recognition as discordant pairs so overall ratios are not important. Of the total of 125 pairs, 85 are concordant, 40 discordant. However, if the number is divided by age all the pairs over the age of 45 (35 pairs) are concordant, i. e. both co-twins are diabetic, where as under this age 50 pairs are concordant and 40 discordant (one twin diabetic, the other unaffected). It is unlikely that the reason for the 40 pairs being discordant is merely that they have not yet had time to become concordant because (a) the gap between the first and second twin developing diabetes in the concordant pairs is usually short - in the majority of cases 3 years or less - whereas most of the discordant pairs have been observed already for a much longer period than this, and (b) the unaffected members of the discordant pairs on repeated glucose tolerance testing over periods of up to 20 years have shown no sign of deterioration. None of the unaffected twins has yet developed diabetes under observation.

The deduction from these results is that juvenile-onset diabetes (i. e. onset under the age of 45 which in most cases means insulin-dependant diabetes) is due, in part at least, to non-genetic factors, whereas diabetes in maturity-onset cases is probably predominantly, or even entirely, genetic in origin. However, even in the juvenile-onset twins there is some genetic predisposition to diabetes since they show the excess of HLA type BW15 which is characteristic of juvenile-onset diabetes. (It is not yet sure whether they show an excess of HLA B8 as well).

If there are non-genetic factors in the aetiology of juvenile-onset diabetes it is clearly of interest to determine what they might be. So far from the twin studies there is no evidence of virus infection as an aetiological agent but this may be merely because the twins were tested too long after the onset of diabetes when evidence of virus infection might have subsided.

Evidence of immune factor in the aetiology of juvenile-onset diabetes comes from the study of islet-cell antibodies. These are found in the majority of newly diagnosed cases and their frequency subsides over the ensuing months. They have occasionally been found as long as 3½ years before the development of diabetes. These antibodies may be an expression of an autoimmune process or the consequence of islet cell damage produced by some other agent, such as a virus.

"Diabetes" is not a single disease but a collection of different disorders all showing hyperglycaemia but in genetic and other respects distinct.

The fact that some juvenile-onset diabetic twin pairs are discordant and seem likely to remain so proves that non-genetic factors must be important in the aetiology of this type of diabetes and therefore gives hope that it may be possible to prevent, ameliorate or even cure it.

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Executive Director's Page

Annual Meeting

The 14th Annual meeting of the National Academy of Medical Sciences was held on the 29th and 30th January 1977. The Chief Guest, Shri C. Subramaniam, Minister for Finance, laid the Foundation Stone for the building of the Academy and granted a sum of Rs. one lakh for the site of the building.

The Council met on 29th January 1977 and Dr. P. N. Chhuttani, Director, PGI, Chandigarh, who had received maximum number of votes amongst the seven candidates for the Presidentship of the Academy, was declared elected as President.

The Council appointed a disciplinary committee with Dr. B. N. Sinha as Chairman and Dr. A. K. Basu and Dr. K. C. Dube as members to deal with disciplinary matters that may arise from time to time and to draft a code of conduct for Fellows of the Academy.

An election dispute committee with Dr. B. K. Aikat as Chairman and Dr. N. Jungalwalla and Dr. I. P. Agarwal as members was also appointed. The committee would prepare draft rules for the election of the President and consider the Jungalwalla-Luthra report regarding scrutinising the ballot papers for the election of Fellows.

The Council further approved the appointment of the Legal Adviser to advise on the affairs of the Academy with effect from 4th November 197o as it was found that many decisions taken are not in the appropriate legal language.

The Council also approved the following at its meeting held on 29th January 1977 :

"The functions of the chapters have already been defined in the Review Body recommendations. They should only confine themselves to local matters.

Functions of the Chapters :

1. The convenors will organise scientific meetings, business meetings and approach the Government for grant.

2. To establish units in the medical colleges in their respective areas.

3. To organise series of lectures, courses and counselling service to the postgraduates regarding MAMS examinations, holding of scientific meetings in each medical college where non-fellows, non-members as well as postgraduate students etc. would be welcome, could be taken up.

4. To have liaison with the University in their areas.

5. To levy fees on Members and Fellows and also levy such fees for the organisation of courses to the students.

6. To appoint faculties with fellows/members and non-fellows/non-members as visiting professor.

7. Any other activities for the advancement of medical science and in the interest of the Academy may be taken up."

Scientific Programmes :

(i) **Orations :** The following orations were given at the Annual meeting of the Academy :

(a) The Academy oration by Dr. S. Padmavati on "Rheumatic carditis".

(b) The Glaxo oration by Dr. P. Brahmayya Sastry on "Studies on human placental acetylcholine and on human lyophilized placenta".

(c) The Lakshmipati oration by Dr. B. N. Balakrishna Rao on "Analysis of Urinary calculi."

(d) The Shriram Memorial oration by Dr. B. Sankaran on "Rehabilitation—Past, present and future."

(ii) **Awards :** (a) The S. S. Misra Memorial Medal plus cash prize was awarded to Dr. Vijay Kumar of P. G. I., Chandigarh, for his paper entitled "Improved ambulatory child care—A simple effective model".

(b) The Sir Shriram Memorial Award for the best published paper during the last three years was awarded to Dr Gurmohan Singh.

Convocation : Twenty Fellows and 16 Members received their scrolls at the 14th Convocation of the Academy. The President outlined the progress made by the Academy during the last two years and mentioned particularly the recognition of the MAMS qualification by the Govt. of India and the Medical Council of India and placing it in the first schedule of the MCI Act which qualifies the members for specialist appointment and teaching posts. She also outlined the efforts of the Academy to obtain inclusion of Medical Education and Health in the Concurrent List in the 42nd Amendment to the Constitution and that the Academy was successful in obtaining the inclusion of the Medical Education at least.

Shri C. Subramaniam in his most stimulating address suggested the Academy to tackle the problems of health the Nation is faced both with regard to fiinding solutions as well as in improving the delivery of Health Care Services to all people. He desired that the Academy should give a new dimension to its outlook and be worthy of the great confidence which has been placed by the Government on it to meet the expectations of the profession and the people.

General Body Meeting : In the General Body meeting on 30th January 1977 lively discussion took place. The Academy has completed 14 years and is still in the adolescent stage getting ready for greater responsibilities.

In inducting Dr. P. N. Chhuttani as the President of the N.A.M.S. the President appraised the audience the great qualities of her successor. Equally gracious was Dr. P. N. Chhuttani's speech in thanking all the Fellows for their trust in him and the worthy past President for all the achievements during her tenure as the President of the Academy. The President stated that he would address all the fellows and members on the future work of the Academy and the N. B. E. which require our immediate attention. The National Academy of Medical Sciences may look forward with confidence for a great future under his able guidance. Let us all help the President to take the Academy to greater heights and make it an Institution of national importance.

— K. N. RAO

Ann Natl Acad Med Sci (India), 13, 1, January—March 1977

In Memorium

Dr. P.K. Haldar, FAMS

Prabhat Kumar (The Morning Glow) who shone on Radiology and carried her steadfastly like a HALADHAR (The able companion of Lord Krishna) over her most difficult and growing stages, passed away on November 23, 1976 at the All-India Institute of Medical Sciences, New Delhi at the age of sixty-one This apostle in the galaxy of brilliant radiologists came to the apex of Oncology group in this country and died in harness through his own speciality.

He was born in Muzaffarnagar on 10th November, 1915 and received his early education in his native state of U. P. Following his early education in science, he entered the King George's Medical College, Lucknow in 1933. After a brilliant career in Medicine, he worked successively as an intern and chief resident in surgery to which he was almost comitted. But through a stroke of instinct, he determined to pursue a career in the then downtrodden and hardly thriving field of Radiology and slowly by-passed into the even more stinking, neglected and marasmic subspeciality of Radiotherapy. By his untiring, indomitable and uncompromising bent of mind, he carried this dying subspeciality to the present scientific form of Radiation Oncology. His affiliation with a number of medical institutions **viz.** Medical College, Agra; All India Institute of Medical Sciences, New Delhi and finally J. K. Institute of Cancer Research of which he was Director till the end, did not confine him to a place nor one institution. Rather he developed a School and a concept in Radiation Oncology in India over the three most useful decades of a mature professional life. Besides all the crown bestowed on him in this country, the Royal College of Radiology conferred on him the prestigious Fellowship early this year. A man of few thumping words and all work, a devoted and illuminating teacher, Prof Haldar remains in the heart of a large number of his students holding key places in Radiotherapy in India. A master of basic sciences, and innovative teaching, having profound command over language and above all, great clinician, he left a piercing impact for future development of Radiation Oncology in India. Only recently he compiled the basic guidelines for Indian College of Radiology of which he was the founder Chairman for furtherance of the knowledge in Radiology. His interests were varied. He is remembered for development of radium application close to radical operations in early stage cancers and particularly professed this treatment in cancers of oral cavity and uterine cervix. He published a variety of papers in Radiological literature and texts. He was a stimulus responsible for development and design of a few radium applicators for cervical cancer in the North India. Prof. Haldar was active in many professional societies which he unstinctingly served. He was a past President of Indian Radiological Association, Chairman of a number of Cancer Committees and Indian College of Radiology.

Prabhat Kumar is survived by his three loving daughters and wife, a superb friend whom he acquired in 1940. The life of this couple was one of enviable devotion and companionship. They have travelled widely across the world and the length and breadth of this country. His knowledge was something more than only Radiology. In his family of fine arts and humanities, whoever tasted his scintillating melodious and yet devine voice is startled and spell bound—"THE VOICE IS NO MORE."

—P. N. WAHI

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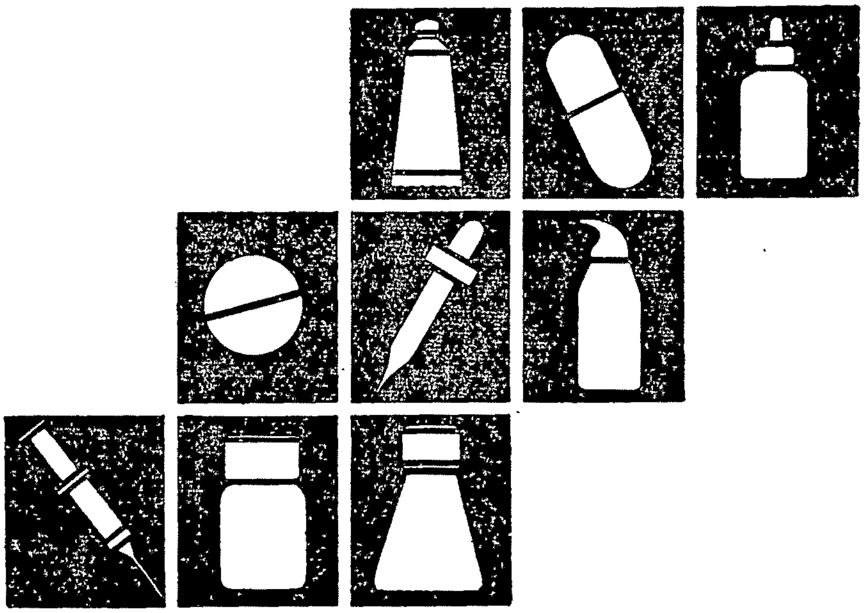

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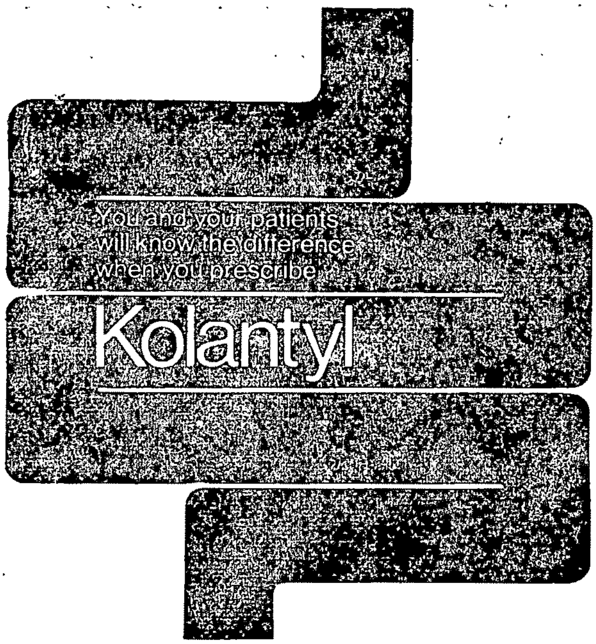

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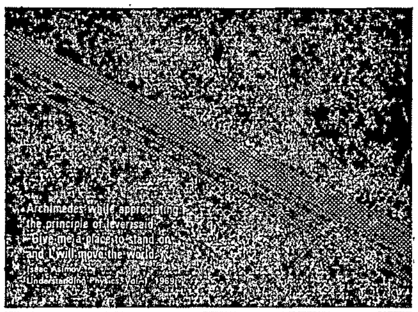

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The Human Body (Its Anatomy and Physiology)
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Ann Natl Acad Med Sci (India), 13, 2, April-June 1977

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Ann Natl Acad Med Sci (India), 13, 2, April-June 1977

Editorial*

Rehabilitation of the Mentally Retarded

Mental retardation is nothing but impaired mental ability. A retarded child learns more slowly than a normal child ; and at maturity the capacity to understand of mentally retarded child will be less than normal. The mentally retarded childern find difficulty in learning, social adjustment and economic productivity. Mental retardation should not be confused with mental illness. As it is not an illness, the question of cure does not arise. It is a life long condition ; however there are conditions sometimes related to mental retardation which can be improved or sometimes cured **e.g.,** deafness, poor vision, emotional disturbance. Poor living conditions may sometimes make a child appear retarded. Early detection can help to lessen the degree of handicap and, therefore, basically mental retardation is mainly a problem of education and rehabilitation. The aetiology of mental retardation may not be known in many cases but nearly 200 known causes are, however, recorded. Retardation can be caused in the pre-natal, natal or post-natal period. Retardation can develop because of a genetic defect. German measles, if contracted by the mother during the first trimester of pregnancy, or excessive drugs or x-ray treatment during pregnancy, can as well cause mental retardation. Birth injury or biochemical disorders in the new born, brain damage caused in infancy and childhood by infective fevers like encephalitis or meningitis are other important causes. Intelligence can be sharply affected if the environment of the child during the early childhood is adverse. The type of environment a child has during the first five formative years of life, can make a considerable difference in intelligence. There are, therefore, a great many causes but few of them are fully understood. Even when we say **how** mental retardation is caused it is rarely possible to determine **why.** There is no data on all India base about mental retardation. Random surveys by several workers place the figures as 1.68 to 18.2 per cent of school going population, and 1.5 to 5 per cent of total rural population. The wide ranges specially in the school going childern are understandable as parameters of mental retardation are not sharply defined or quantified.

On the basis of the WHO Report (1968) and extrapolating these figures to the Indian population, we will have, on a most conservative estimate, not less than 2 million in the group of the adolescent and adult retarded who need special services in the form of prevocational training and vocational rehabilitation. Chronic schizophrenics who fill more than 50 per cent of our mental hospital beds and stay for indefinite periods or vegetate at home for want of rehabilitation services, will again on a conservative estimate constitute another 2 million. Thus, we have approximately no less than 4 million people in the population who are physically well and who are in the age groups where they can be trained for some kind of vocation and helped to hold a remunerative job in a sheltered environment if not in the open public market. While paucity of financial and manpower resources may account for a small part of our lack of attention to the needs of this handicapped group of people, this is not the sole reason for social apathy. To a certain extent this may be due to the fact that whereas physical handicap elicits sympathy, mental retardation elicits fear, ridicule or aborrhance which to a certain extent may be due to irresponsible, chaotic or socially disapproved behaviour of the afflicted, coupled with lack of understanding of the genesis of the trouble by the society at large.

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*The views expressed in the editorial are the personal views of the writers and are not necessarily the views of the Academy.

In addition to this emotional resistance to the ideas of rehabilitating the mentally handicapped, another factor which has been responsible for our half-hearted attempts at rehabilitating the mentally handicapped, is our lack of faith in their rehabilitability, especially in the vocational sphere. This is well reflected in the popular reference for a slack or poor worker as 'Idiot' or 'Budhu'.

Actual experience, however, has shown that the mentally handicapped can be trained to carry out work of varying degrees of complexity. Chronic schizophrenics and the mentally retarded in Mapperly Hospital in Nottingham, U.K., have been known to turn out such exquisitely finished christmas decorations, that they are not able to cope with the bulk of orders. Remploy Ltd., U.K., where the employees, apart from the Secretarial and Supervisory staff, are all physically and mentally handicapped people, make suitcases, furniture and other articles which compare favourably in the open market, with products manufactured by normal people. With the present day emphasis on teaching machines, programmed learning and advances in behaviour modification techniques, the possibility of teaching desired items of behaviour for the mentally handicapped, in the social and vocational sphere, has become considerably enhanced and this in turn, has made rehabilitation efforts more fruitful and satisfying. It is, however, true that the majority of the mentally hahdicapped can work only in a sheltered work where skill needed for adjustment to changes in situation are minimal. The results of placing them in open employment have not been very encouraging, though, very often the supervision and protection they need is minimal.

Basically, the primary prevention relates to measures which prevent the intial occurrence of the handicap. This is effected most directly through control of environmental factors which may injure the child before, during and after birth. The maintenance of high standards of antenatal care, skilled attention during child birth, satisfactory nutrition and vastly improved control of infection in the infant are needed here. Negative eugenic measures are hard to apply and are at present of slight practical importance. However, genetic counselling, at least with regard to some of the clear-cut syndromes of subnormality should definitely be available to the community. In case of single gene inheritance, where the mode of inheritance of the clinical entity is known, intelligent and inquiring adults may be given the facts about the expectation of abnormality in their offspring which will enable them to decide for themselves about marriage and birth control. In this respect the public education is of obvious importance. The secondary prevention relates to early discovery, diagnosis and early care and treatment of the mentally retarded. This is of prime importance in those syndromes where treatment is possible as for instance in cretinism, galactosaemia, phenylketonuria, diabetes, insipidus and syphilitic infection.

The vocational rehabilitation of mentally retarded is not bereft of benefit to the society. Its benevolent act will be repaid by canaling a social burden group into a productive one. The task is not a simple one. Special individual attention will be required based on age, functional intelligence, associated physical disability, if any, and also on job opportunities.

Assembly-line type of machine-work, packaging envelope making, labelling, weaving, carpentry, tailoring, farm work etc., have all been usefully employed for rehabilitating the mentally retarded, depending on the local availability and type of subcontract work in the region etc.

The total task requires co-ordinated activity by State machinery, voluntary organisation and academic bodies. Industries can play a major role in the vocational rehabilitation of the mentally handicapped by offering subcontract work to the institutions training the retarded, starting training centres in their workshops, themselves, reserving some posts for the mentally retarded exclusively and operating sheltered workshops for them as annexes to regular workshops for the normal.

The government, in its turn, has to address itself to the question of training personnel in the field of rehabilitation, establishing vocational training centres for the mentally handicapped and sheltered workshops for those who need long-term placement in sheltered work environment, and framing legislation to ensure that those among the mentally handicapped who are able to work productively are given opportunity to find themselves places in the labour market under a quota system.

Ann Natl Acad Med Sci (India), 13, 2. April—June 1977

Chemotherapy of Malaria

Nitya Anand*

Central Drug Research Institute, Lucknow.

Although the malaria eradication programme had shown very impressive gains, the resurgence of malaria in the past few years, in areas where it appeared to be totally eradicated, has emphasized the fact that a more pragmatic approach would be to plan for control and containment of malaria rather than aim at its total eradication (WHO, 1969). Obviously drugs, both for therapy and prophylaxis, form a most important component of such control measures. The potential usefulness of chemotherapy in all phases of treatment of malaria has now been fully recognised (Bruce-Chwatt, 1972; WHO, 1967, 1973). Even the use of available drugs would go a long way in decreasing the toll of death and morbidity due to malaria. However, the success of chemotherapy would be greater if drugs are available which would be effective against: (1) all the developmental stages of the parasite and thus prevent relapse, (2) drug resistant forms, (3) different species of the parasites, and (4) be long acting.

Present Status

The drugs presently used in the treatment of malaria act at different stages in the life cycle of the parasite and vary in effectiveness. The female anopheles mosquito introduces sporozoites, the infective stages of the malarial parasite, into the human host and within 15-30 min. these enter into the parenchymatous cells of liver where they multiply by nuclear division to give rise to merozoites. The pre- and exo-erythrocytic merozoites enter the red blood cells and grow to mature schizonts which by nuclear division give rise to merozoites. Some of the merozoites on entering the red blood cells develop into male and female gametocytes which constitute the sexual stage. These gametocytes when taken in by a female anopheles mosquito develop into male and female gametes which fuse and ultimately give rise to infective sporozoites. The cycle is repeated.

There are a number of species of malarial parasite responsible for infection in humans. In India the infection is due mainly to **P. vivax** with pockets of **P. falciparum** infection particularly in the north eastern region.

Antimalarial chemotherapy includes suppressive treatment and radical treatment. Suppressive treatment implies prevention or suppression of clinical symptoms by the action of a drug on blood parasites and may be divided into 'presumptive' treatment, which is an essential part of surveillance activity and mass drug treatment. Radical treatment aims at a complete cure of confirmed malaria cases and is intended to prevent relapses. Depending upon the species of the parasite, radical treatment may require action against the erythrocytic form, secondary exoerythrocytic form, or both.

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*Director

The more important drugs currently used in prevention and cure of malaria and the stage at which they act in the cycle of infection are given in the Table. As is apparent from the table, each class of drugs has a different set of characteristics in relation to the species of the malarial parasite and its phase of development, which affect the speed of action and toxicity and thus their use.

Table. Effect of drug on different stages of malarial infection of P. Falciparum and Vivax

			Human	Host		
	Drug	Mosquito (Sporonticidal Drugs)	Tissue (causal prophylactic and Antırelapse Drugs)	Blood (Schizonticidal and Gametocytocidal Drugs)		Radical cure
		Oocysts Sporozoites	Pre- and Exo-Erythrocytic Merozoites	Schizonts and Merozoites	Gametocytes	
I.	Quinine	—	—	++	+(vivax)	+(falciparum)
	Mepacrine	—	—	++	+(vivax)	+(falciparum)
II.	**4-Aminoquinolines**					
	Chloroquine	—	—	++	+(vivax)	+(falciparum)
	Amodiaquine	—	—	++	+(vivax)	+(falciparum)
III.	**8-Aminoquinolines**					
	Pamaquin	++	++	+	++	+
	Primaquin	++	++	+	++	+
IV.	**Dihydrofolate Reductase Inhibitors**					
	Proguanil	+	+	+	+	+
	Cycloguanil	+	+	+	+	+
	Pyrimethamine	+	+	+	+	+
V.	**PABA antagonists**					
	Dapsone	+	+	—	—	—
	Sulfalene		+	—	—	—
VI.	**Miscellaneous**					
	Tetracyclines	—	+	+	+	+

Quinine is a highly active blood schizonticide and can produce radical cure n **P. falciparum** infection. As it has no effect on the exo-erythrocytic stage, it can not prevent relapse in **P. vivax, ovale** or **malariae** infections. It has got gametocidal action against **P. vivax**, **ovale** and **malariae** but not against **P. falciparum**. The use of quinine declined with the introduction of synthetic anti-malarials, but with the emergence of drug resistant plasmodia strains, especially of **P. falciparum**, it is being widely used again. The precise mode of action of quinine is still unknown. It can intercalate with DNA but it is not certain if this is the cause of its antimalarial action. Quinine can inhibit the chloroquine-induced clumping of hamozoin.

Quinacrine was the earliest synthetic antimalarial to find widespread clinical application. But because of its toxic side-effects following prolonged administration, its use has been severely restricted in recent years. It is a potent schizonticide of all species of malaria, has some action on the gametocytes of **P. vivax** and **malariae**, but has no action on any other stage.

4-Aminoquinolines are very effective against asexual erythrocytic forms and thus are very valuable in the rapid control of acute attacks of malaria. They have some action against the gametocytes of **P. vivax** and **P. malariae**. Since they act primarily as blood schizonticides they do not prevent relapse of **P. vivax** malaria and produce radical cure in **P. falciparum** infection only. Chloroquine causes a disruption of the digestive process of the parasite, leading to acute amino acid deprivation and cytolysosome formation. Breakdown of the ribosomal RNA in the intact organism after chloroquine therapy is a consequence of autolysis inside the cytolysosome that is formed within the parasite on exposure to the drug. It is believed that intercalation with parasite DNA is likely to follow only when the internal organisation of the drug exposed parasites has been completely disrupted and free drug is released within the general parasite substance.

A saturable receptor site in the strains of **P. berghei** and **P. falciparum** sensitive to chloroquine has been demonstrated by Fitch (1970). This receptor site is lost when resistance to chloroquine develops. Rapid clumping of hemozoin is observed on exposure to 4-aminoquinolines and quinacrine. This clumping is in some way associated with the concentration of the drug in the parasite.

8-Aminoquinolines have poor action against the asexual erythrocytic stage of the parasite, but kill the gametocytes and the exo-erythrocytic forms in the liver, thus rendering the host incapable of infecting the mosquitoes and producing a radical cure of the infection. Primaquin is less toxic than pamaquin and is used extensively for radical cure and as a causal prophylactic of vivax malaria. Primaquin has also a potent sporonticidal action but is normally not used for this purpose because of its possible side-effects. The mode of action of 8-aminoquinolines is considered to be due to disruption of the function of mitochondria and structures having mitochondrial function present in the malarial parasite which can synthesise ubiquinone.

The dihydrofolate reductate inhibitors (pyrimethamine, proguanil, cycloguanil) are effective against exo-erythrocytic forms of **P. falciparum** and **vivax** and against blood forms. They are also active against chloroquin-resistant strains of **P. falciparum.** They prevent the production of infective sporozoites in the mosquito and can be used as causal prophylactics. They act slowly and have a flat dose-response-curve. Their action is plasmodistatic rather than plasmodicidal. Drug resistance is common in them. These compounds bind selectively and inhibit dihydrofolate reductase, an essential enzyme in the folic acid pathway (Gregory and Peters, 1970). The strength of binding of the different analogs to this enzyme from different sources varies considerably and the choice of the drug is dependent upon this binding strength. Pyrimethamine binds much more strongly to DHFR from the malarial parasites than from a bacteria, while the opposite is the case with trimethoprim. Pyrimethamine is therefore the favoured drug for treatment of malarial infections.

Sulfones and sulfonamides show considerable activity against blood forms, and can be used both as prophylactics and curatives. They are active also against chloroquin-resistant strains; they are more active against **P. falciparum** than **vivax.** Their action is potentiated by combination with pyrimethamine. They have a definite place in the treatment of infections with aminoquinoline-resistant strains.

PABA is incorporated at the first step in the formation of folic acid. Sulfonamides and sulfones competitively inhibit the enzymes involved in the incorporation of PABA. The dihydrofolate reductase inhibitors and sulfonamides/sulfones act at different steps in the folic acid pathway, which explains their synergistic action and rationale for their use in combination (Anand, 1975).

Antimalarial activity of antibiotics, both as regards relief from symptoms and clearance of parasitaemia, is slower than that of standard antimalarials. But because of appearance of drug resistance to chloroquine, antibiotics are being tried again. It has been shown that 250 mg. of tetracycline hydrochloride given 6 hourly for 7 days cured 13 of 14 **P. falciparum**-infected volunteers (Colwell **et al** 1972). Derivatives of tetracycline like doxycycline and mimocycline have been reported to give even better results (Clyde, 1971). There is need to reassess their status in antimalarial chemotherapy.

Thus, for suppressive treatment the generally accepted drugs are 4-aminoquinolines, pyrimethamine and primaquin, used singly or in combination given in a single dose or weekly. Administration of salt medicated with these drugs has also shown promise for mass treatment. For radical treatment of falciparum and vivax malaria, 4-aminoquinolines and primaquine, alone or in combination, are used. For chloroquin-resistant strains antifolics (and primaquin) can be used with advantage.

Repository antimalarial drugs : Though quite a large number of antimalarial drugs are available, they are effective only for brief periods and frequent administration is required. This creates problems in malaria control programmes, particularly in countries like India with a large widely spread rural population and with inadequate medical and public health facilities. In such a situation it would be most useful to have a repository, single-dose, oral or parenteral, well-tolerated drug, which could afford protection against sensitive and drug-resistant parasites for many months. The two basic approaches towards the development of such drugs have been to synthesise antimalarials which will get fixed in the tissues and then be slowly released, and to prolong the action of known antimalarials by delaying their degradation and excretion or by reducing their rate of absorption. Derivatives of some of the major classes of antimalarials have been made which are likely to be long-acting. Three preparations which have shown the most promise as repository drugs are cycloguanil pamoate or embonate, 4,4'-sulfonylbisacetanilide (acedapsone) and a mixture containing equal parts of cycloguanil and acedapsone (Elslager, 1969).

A single 5 mg./kg. intramuscular dose of cycloguanil pamoate was shown to protect human volunteers for 8-12 months against subsequent challenges with **P. vivax** (Powell **et al**, 1965) or **falciparum** (Contacos, 1964). For prophylaxis against malaria it may be repeated every 4 months. One of the important results of these studies is the demonstration that an extremely small amount of an antimalarial drug can prevent the growth and possibly even the survival of malarial parasites when they are constantly exposed to the drug over long periods.

Human malarial parasites vary greatly in sensitivity to sulfones; **P. falciparum** is very sensitive while **P. vivax** is not. Therefore, acedapsone alone has not been studied extensively in human malaria.

An acedapsone-cycloquanil pamoate combination has been found very useful in clinical antimlarial studies, especially against drug-resistant strains (Chin **et al**, 1967). Long-acting antifolics do have a definite place in antimalarial chemotherapy. However, the possibility of inducing concomitant resistance to bacteria can be a major problem and limits their widespread use. Cycloguanil pamoate-acedapsone combination given parenterally at 4 month intervals can be used with advantage: (1) for attack and consolidation phase of the malaria eradication programme, (2) for protection of migrant population, and (3) as a causal prophylactic (Elslager, 1969). This form of treatment would offer a logistic advantage in countries like India. There is need to carry out a well planned field trial with this combination in India.

Drug Resistance : The prevention and management of drug resistance is one of the important practical problems of malaria control. Although so far the only species of parasite of importance to man that has developed resistance to a significant degree is **P. falciparum** to chloroquin and dihydrofolate reductase inhibitors, the possiblity of resistance developing in **P. vivax** can not be ruled out. Some strains of **P. vivax** having resistance to antifiolics have been reported.

It is necessary to distinguish drug resistance from drug failure. Drug resistance is the ability of a parasite strain to multiply or survive in the presence of a concentration of a drug that would normally destroy parasites of the same species and this resistance may be relative or complete. While drug failure is the absence or insufficiency of drug action which may be the result of improper ingestion, deficient absorption, unusual rate of degradation or rapid excretion of the drug.

In any malaria control programme it is necessary to keep surveillance on the development of resistance, its degree and distribution limit, and try to eliminate the existing foci of resistance, and also to develop alternative drugs for resistant forms.

The mechanism of development of resistance to antifolics is reasonably well established and is related to decreased binding affinity of the enzymes involved (Ferone, 1970) and in some cases to increased production of PABA (in case of sulfonamides and sulfones) by the parasite. Cross-resistance normally extends beween dihydrofolate reductase inhibitors or sulfones and sulfonamides, but these resistant strains generally respond to a combination of the two types of antifolics. However, strains of **P. falciparum** resistant to this combination have been reported, which would serve as a strong caution against the injudicious use of this type of combination on a large scale. The mechanism of transmission of resistance is not definitely known; it has been suggested that the resistance is carried on multiple genetic foci, and transfer factor may be involved in its transmission.

Various hypothesis regarding chloroquin are based on two observations with resistant strains of **P. berghei**. Firstly there is decrease in the chloroquin uptake of red cells parasitised with the resistant strain as compared with the sensitive strain. Secondly, there is apparent change in the respiratory function of resistant parasites. Fitch (1969, 1972) showed a marked reduction in the ability of chloroquin-resistant

P. berghei to concentrate chloroquin, and it has been postulated to be due to deficiency of high affinity binding sites in the parasites. Homewood **et al** (1972) suggested that resistant strains may have less acid food vacuoles in comparison to sensitive strains and consequently take in less chloroquin. Based on the second observation Howells **et al** (1970), proposed that chloroquin resistance is due to the ability of certain parasites to switch on prematurely aerobic pathways of respiration. It seems likely that the mechanism underlying chloroquin resistance is inherent in a genetic mutation that is expressed when drug selection pressure is exerted.

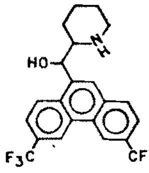
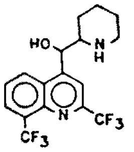
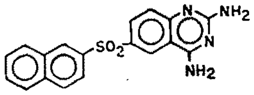
New Antimalarials: Antimalarial drugs currently available have a number of shortcomings, the most important of which are: (i) No single drug is equally effective against different species of the malarial parasite, nor is any single drug effective against all stages of the parasite and thus none of the drugs is equally suitable for prevention and treatment of malaria; (ii) increasing incidence of the development of drug resistance especially against 4-aminoquinolines, still the most widely used group of compounds; (iii) the need to administer the drugs at short repeated intervals to a large proportion of the population, which is very difficult particularly in rural areas with widely scattered population and rudimentary health services.

Recent reports of the appearance of strains resistant to various known drugs has further focussed attention on the need for new antimalarials. As a part of the military needs of the Vietnam war, the U. S. Army launched a massive screening programme for discovery of new drugs, and the Walter Reed Hospital screened around a quarter of a million compounds in this programme. A number of compounds have emerged from this programme as potential candidates for detailed clinical evaluation; the most imortant ones are given in Fig. 1. These compounds, although belonging to the same classes of compounds which are already known, have a higher order of activity, and are also active against the resistant strains. WR 158122 seems particularly promising. It is active at a very low dose and is effective against some of the resistance strains of plasmodia. Though structurally it resembles both DHFR inhibitors and sulfones, it is mainly a DHFR inhibitor. However, resistance to this drug also develops rapidly, and this appears to be a major draw back with this drug. It may find greater use in combination therapy.

The relatively small number of new compounds that have emerged from this massive screening programme, would show that broad screening is perhaps not the right approach to the discovery of new and better antimalarials. It appears necessary to devote greater attention to the understanding of host-parasite relationship, and to know specific biochemical requirements of the parasites in different developmental stages and the factors responsible for change from one stage to the other, which would provide a rational basis for design of drugs.

Fig. 1

OTHER PROMISING COMPOUNDS

COMPOUND	STAGE OF EFFECT	EFFECT ON RESISTANT STRAINS	DEVELOPMENT OF RESISTANCE	DOSE mg/kg
 WR 122455	Schizonticide	+	Slow	2.5 for 7days
 WR 142490	,,	+	–	Single dose preferred
 WR 158122	,,	+	Rapid	0.025 for 7days 0.0062 in combination with sulphas

Conclusions

(1) The screening programme for new drugs should be organised as a national programme. At least at one centre in the country facilities should be set up for primary to tertiary screening including testing in owl monkey for human malarial infection, and upto the stage of clinical pharmacology.

(2) Chemical work done in university chemical laboratories should be made use of in this screening programme.

(3) In development of new chemotherapeutic agents the main emphasis should be on: (i) causal prophylactics active against sporozoites in human host, (ii) gametocytocidals to prevent transmission of infection, and (iii) agents acting by new mechanisms to overcome problems of resistance.

(4) Drugs with repository action and new delivery systems to release drugs slowly should be developed.

(5) A field trial should be carried out in India with a cycloguanil embonate/pamoate-acedapsone combination.

(6) A constant surveillance should be kept for development of resistance under field conditions in India.

(7) Greater emphasis should be laid on basic biochemical studies in this field to plan for more rational basis for chemotherapy. University laboratories should also be involved for this purpose.

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Problem of Drug Resistance in the Control of Malaria

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During the last three decades the most commonly used antimalarials either as therapeutic or prophylactic are the Aminoquinolines (4-amino and 8-amino), Diaminopyrimidines (Pyrimethamine) and the Biguanides (Proguanil). All these had replaced the earlier antimalarials **viz.** Quinine and the Aminoacridines. All these antimalarials are often classified into 5 groups based on their action as follows :

(i) **Causal Prophylactics or Primary tissue schizontocides** : (Primaquine, Pamaquine, Pyrimethamine and Proguanil).

(ii) **Schizontocidal drugs or Blood schizontocides** : Quinine, Mepacrine and the 4-aminoquinolines.

(iii) **Gametocytocidal drugs** : (8-aminoquinolines)

(iv) **Sporontocidal drugs** : (Proguanil and Pyrimethanine)

(v) **Antirelapse drugs or secondary tissue schizontocides** : (8-aminoquinolines)

The 4-aminoquinolines, the 8-aminoquinolines and Pyrimethamines have been in extensive use all over the world for the treatment of malaria as also in the malaria eradication programmes of various countries. In India also these drugs have been in use under the NMEP since 1958 and have contributed to a very great extent in bringing down the incidence of malaria. These drugs continue to be effective instruments in the control of malaria in many parts of the country. However, in certain pockets in the Eastern part of the country where a strain of **P. falciparum** is resistant to chloroquine the need for an alternate drug is felt.

Problem of Drug Resistance : Chloroquine resistant **falciparum** has been recognised since 1960 in parts of South East Asia, S. America and Central America. Studies since 1973 in different parts of India by the National Institute of Communicable Diseases, Delhi and the National Malaria Eradication Programme, have shown that a strain of P. **falciparum** resistant to chloroquine is present in some localities of Assam, Meghalaya and Mizoram. Resistance and sensitivity to drugs are not absolute

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qualities. Between full sensitivity and complete resistance there is a gradation from a loss of effect demonstrable only by occasional recrudescence to a resistance so marked that the drug has no effect in severe infections. The grading of resistance by means of the W.H.O. Standard test (W.H.O. 1968) is as follows :

Response	Recommended Symbol	Evidence
Sensitivity	S	Clearance of asexual parasitaemia within 7 days of treatment, without subsequent recrudescence.
Resistance	R I	Clearance of asexual parasitaemia as in sensitivity, followed by recrudescence.
	R II	Marked reduction of asexual parasitaemia but no clearance.
	R III	No marked reduction of asexual parasitaemia.

The tests so far carried out show that resistance is only of a moderate level-RI and RII in Assam, whereas in some parts of Meghalaya 12.5 per cent of the cases are of RIII level. The objectives to be achieved in the control of drug resistant malaria summarised by WHO are as follows :

1. Confirmation of the presence of resistance, and determination of its degree and distribution as quickly and reliably as possible.
2. Elimination of existing foci of resistance, and increased vigilance in such areas.
3. Quick and effective limitations of the spread of the resistant strain.
4. Planning of future activities so that alternative effective drugs are available for radical cure and for prevention of transmission.

The above mentioned objectives are under the active consideration of the NMEP in India.

Chemotherapy of Chloroquine resistant falciparum Malaria : In vast areas where resistance of **P. falciparum** to 4-aminoquinolines has been observed, these drugs still serve a very useful purpose because they are effective against :

(a) infection by other species of malaria parasites, and

(b) those infections with strains of **P. falciparum** that are not resistant and are often widely distributed in the area. Also some strains or infections with a low degree of resistance respond well to an increased dosage of 4-aminoquinolines or to their repeated administration.

In areas where resistance to 4-aminoquinolines is marked and widespersed the use of alternative drugs will have to be considered. The treatment of Chloroquine resistant **falciparum** malaria has hitherto been confusing. No clear cut regimen has yet emerged (Lancet 1971). The World Health Organisation (1973) has mentioned 16 different regimens involving 12 drugs administered over one to 14 days.

Canfield and Rozman (1974) have reviewed the trials with 26 new anti-malarial compounds and have found that 2 compounds **viz.** 4-quinoline methanols and 9-Phenanthrenemethanols have greater activity against drug resistant **P. falciparum** than any other known drug. They have also reported that several other compounds presently being tested in human subjects are even more potent. Clyde (1974) has stated that resistance to 4-aminoquinolines may be met curatively with courses of treatment lasting 1-14 days or more, the longer courses relying on quinine, often with sulfonamide or on tetracyclines, and the shorter courses on associations of sulfonamides or sulfones with pyrimethamine or trimethroprim.

In U. S. A. alone more than 215,000 compounds have been reviewed and tested for their effect on plasmodia (Lepes 1974). Of these, only four deserve further clinical and field trials. They are : (a) derivatives of 9-phenanthrene methanols, (b) 4-quinolinemethanols, (c) 2,4-diamino-6-Sulphur substituted quinazolines; and (d) 1-benzoxy-alloxy-4,6-diamino-S-triazines.

A study by Hall **et al** (1975) in Thailand has shown that Quinine and Fansidar (Sulfadoxine-Pyrimethamine) is promising. They have recommended after trials on over 300 patients Quinine 540 mg. (2 tablets of 270 mg. each) every eight hours atleast four doses followed by Fansidar (each tablet containing 500 mg. Sulfadoxine and 25 mg. Pyrimethamine) 3 tablets given with or eight hours after the last dose of quinine.This regimen cured 96 per cent of patients (302/314). The quinine brings the infection under control and fansidar aids its eradication. Fansidar is non-toxic when given at the end of the course of quinine.

For Chloroquine resistant **falciparum** malaria quinine is the only rapidly acting drug currently available.

Research studies to be taken to combat the resistance problem : There is an urgent need for a more through monitoring to demacrate the precise extent of the problem.

In vitro tests for resistance developed by the WHO (test kits for these are now made available) should also be undertaken to ascertain the correlation between **in vivo** and **in vitro** results.

Further clinical and field trials on the following 4-compounds are necessary. They are : (a) derivatives of 9-phenantherene methanols; (b) 4-quinolinemethanols; (c) 2,4-diamino-6-sulphur substituted quinazolines and (d) 1-benzoxy-alloxy-4,6-diamino S-triazines.

Basic research on the biochemistry of the malaria parasite and the mode of action of antimalarials and the factors involved in drug resistance.

Research on the dynamics of drug resistance and on the value of drug combinations in preventing or delaying its emergence.

The susceptibility of the different vectors of malaria in India to the resistant strain of **P falciparum** so that a forecast of the likely spread of the resistant strain can be made.

Studies on suppressive prophylaxis with new compounds like acedapsone, sulfadoxine, sulfalene, diformyldapsone **etc.**, should also be taken immediately.

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Vector Control Methods for Malaria

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Malaria continues to be the major disease transmitted by anopheline mosquitoes in India and thus started challenging the progress of the country. Attempts to eradicate this infection have been to undertake measures against vector species. The methods which were primarily based on the use of synthetic insecticides against mosquito vectors have reached a state of crisis and the eradication of malaria does not seem feasible in the foreseeable future. This situation has arisen due to emergence of insecticide resistance in mosquitoes and the adverse ecological effects resulting from the large scale use of these chemicals.

Current status of vector control measures : The advent of DDT and other synthetic residual insecticides about 36 years ago completely revolutionised the concept of control of arthropod borne diseases. These chemicals not only gave quick results but because of broad spectrum of action were also considered the insecticides of choice in malaria eradication.

Dramatic results were achieved in the initial stages and interruption of transmission was achieved in large areas of the country. This excellent progress was maintained till 1964-65. Thereafter the programme suffered setback due to various reasons. Since then, various remedial measures have been taken but all these have failed to stem the rot and the incidence of malaria has been rising steadily. According to the latest figures, 51,66,142 blood smears were found positive for malaria during 1975**.

Reverses were mainly due to the development of resistance to DDT or HCH or to both in two of the major vector species **viz. A. culicifacies** and **A. stephensi** (Sharma, 1972). Delay in receipt of insecticides and delay in change over to alternate insecticides in areas showing resistance to DDT led to the worsening of the epidemiological situation. In areas where the vector was resistant to both DDT and HCH, change over to malathion has not been easy due to its exorbitant cost (16 times costlier as compared to DDT operation-wise).

With the programme extending over more than 20 years and repeatde and continuous insecticidal pressure the problem of resistance has spread over 12 States of the country covering an area of about 0.97 million sq. km. and with a population of over 145 million. Resistance to HCH is also spreading fast and many areas have no practical and economic alternative in view to tackle the problem successfully. Even in areas with no resistance problem the present high cost of insecticides prevent their large-scale use. Other methods of vector control through anti-larval operations, are also being studied but these approaches to combat rural malaria are too costly to permit their adoption.

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**It is understood that over six million cases were reduced in 1976.

In the eastern parts of the subcontinent where **A. minimus** was the primary vector, the operations under National Malaria Control Programme (NMCP) and National Malaria Eradication Programme (NMEP) almost eliminated this species. But lately in these areas **A. philippinensis** has become a major vector as also with **A. balabacensis** in forested areas. Both these species, though susceptible to DDT and HCH are not easily amenable to conventional control methods with residual insecticides owing to their exophilic as well exophagic habits. In these areas, interruption of transmission has not been possible even with excellent insecticidal coverage in time and space.

Since 1963, the problem of urban malaria has been increasing. Resistance of **A. stephensi** to DDT and or HCH is not of great significance, as use of residual insecticides for **A. stephensi** control in urban areas is not resorted to. The emphasis in these situations is on larval control with larvicidal oil, paris green, abate and larvivorous fish. Adulticidal measures against **A. stephensi** are restricted to space spray with pyrethrum. Good results have been achieved by the use of larvivorous fish **viz.** Gambusia and 'Guppy' in certain towns of Andhra Pradesh and Maharashtra particularly in Bombay.

Alternate control strategies : In view of the limitation and scope of residual insecticide for the control of arthropod borne diseases, and the need for development of integrated control measures with particular reference to India have been discussed in detail in recent years, a special task force appointed by the Government in 1973 has strongly recommended the need for finding out suitable genetic and biological vector control methods (N.I.C.D. 1973). A high powered committee appointed by the Government in 1974 to review the working of NMEP has recommended a change in strategy from eradication to selective control, as control seemed to be a more realistic goal than eradication of malaria (N.I.C.D. 1974). For achieving good control, it becomes imperative to add new weapons to the arsenal to combat malaria before further progress could be expected. Therefore, there is strong need to gear up researches for evolving new strategies, which can profitably be undertaken in the following directions.

i) **Source reduction :** Such an approach will involve minor and major engineering measures and improvement in enviromental sanitary conditions for suppression of vector populations.

ii) **Biological control :** The biological control methods aim at the use of natural parasites, pathogens and predators for the reduction of mosquito populations. The most promising methods of control are as follows :

(a) **Larvivorous fish : Gambusia affinis** the 'top minnow' has already made a mark in achieving biological control of mosquitoes. Control of **A. stephenis** in Bombay is a classic example. Similarly, **Pocillia reticulata** has also done a remarkable job for the control of **C. P. fatigans** in Maharashtra and Gujarat States.

There is a strong need to carry out a complete survey of native fauna of larvivorous fish in different parts of the country to obtain comprehensive information on their biology and ecology with a view to determine their potential as biological control agents.

(b) **Parasitic nematodes :** Several species of parasitic nematodes, notably mermithids are known to attack mosquito larvae in nature. **Mermithids nema** (or roundworm) spend part of their life cycle as parasites in the body cavity of their host and rest as free living worms. Very promising results have been achieved with **Reesimermis nielseni** and results of field trials being conducted by the W.H.O. are awaited with great interest. There is a great potential in determining the local **mermithid** fauna and the susceptibility of vectors species of malaria to them.

(c) **Parasitic protozoan : Microsporida** are the common protozoan parasite known to cause disease in mosquito. **Microsporida** belonging to genus **Nosema** seem to have great potential for use in malaria control programme, as anopheline mosquitoes appear to be their primary hosts. Furthermore mosquitoes heavily infected with **Nosema** are known to inhibit the growth of malaria parasite as compared to the non-infected mosquitoes.

(d) **Parasitic fungi :** Parasitic fungi are an important group of fungi parasitizing mosquitoes with high potential as mosquito control agents. **Coelomomyces** is one which has been extensively studied which is known to infect mosquitoes only. Once established the fungus may be able to maintain itself in the habitat for many years. There is need to detect the species of **coelomomyces** occurring indigenously, develop a method to mass produce them to devise a practical way for their distribution in the field, determine their specificity to individual species of mosquitoes, and obtain toxicological information on the non-target organisms including man.

(iii) **Genetic control:** The basic idea of genetic control is to produce reproductive failure in the natural mosquito population. This can be achieved by releasing sterile or incompatiable males. Also mosquitoes with altered genetic material can be used to control their own species.

Considerable work has been carried out in India under the ICMR/WHO collaborative project for the control of **C. fatigans** and **Aedes aegypti**. Limited feasibility studies carried out in Delhi have shown some promising results. Regarding anopheline control, there are nine anopheline vector species transmitting malaria in different parts of the country. **Anopheles culicifacies,** the chief vector has defied all efforts even for its colonization. However, Vector Control Research Centre of the Indian Council of Medical Research has already embarked upon the development of suitable techniques for the control of **Anopheles stephensi,** the vector species for urban malaria in some cities. These techniques are under various preliminary stages of development in the laboratory.

(iv) **Chemical Control :** Chemical control still remains the method of choice for obtaining effective control of any vector/pest species. It is desirable to always look for alternate cheaper chemicals with minimal toxic hazards which may be utilized effectively in combination with other methods of control.

(v) **Integrated control**: Integrated control means the judicious combination of different control measures in such a way that they can be used in the field harmoniously with the prevailing ecosystem of the species. The system envisages; (i) avoidance of loss of effectiveness of established natural enemies complexes by applying the insecticides at appropriate time with appropriate formulation so that only the target species is largely destroyed and (ii) direct or indirect manipulation of natural enemies with a view to suppress the vector population.

The method looks very simple but it is most complex and challenging. For the success of this approach the research studies should be vigorously started on the on following lines:-

Extensive studies on the biology of each vector species should be undertaken in the areas of their distribution by selecting an appropriate index area ;

Such studies should also be extended to other non-target species and other components of the ecosystem. Extensive studies should also be undertaken on the human ecology with particular reference to agricultural practices and living conditions having bearing on the vector population.

Such knowledge will go a long way in effectively utilising other methods of vector control in an integrated way to the fullest extent.

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Immunoprophylaxis in Malaria

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Malaria has been and potentially still is one of the greatest killer of mankind in India. During pre-partition period the malaria morbidity was 7.5 crores and deaths due to malaria were nearly 8 lac a year. With the launching of National Malaria Eradication Programme in 1958, the malaria morbidity in the country was reduced to 100,000 during 1965 as compared to 7.5 crores a year during pre-partition period. Similarly deaths due to malaria were completely eliminated. But unfortunately during 1974, 31 lac cases of malaria have been reported. Consequently it is a serious concern for all that a disease which was on the way to eradication has reappeared in a big way. This is because of complacency as regards vigilance and discontinuance of further research on malaria. Moreover the development of resistance of some malaria vectors to the available cheaper insecticide, nonavailability of adequqte quantity of appropriate type of insecticides, resistance of P. **falciparum** infection to 4-Aminoquinoline in certain areas and financial constraints have been further contributing factors. Consequently one has to look for other remedial measures like immunoprophylaxis which would be more suitable for mass adoption in an economically poor, developing country like India. By this means not only the entire population can be protected against malaria but its transmission also would be stopped.

Evidences of immunity: The possibility of the immunological control of malaria was indicated by both clinical and experimental observations of malarial infection which is well summarised in a recent W.H.O. Technical Report (WHO, 1973). "The acquisition of resistance to malaria in man has been inferred from such observation as the relative resistance to reinfection (and lower levels of parasitaemia) of long-term residents of endemic areas as compared with previously unexposed individuals and their relative lack of clinical signs and symptoms despite persistent parasitaemia. Infection may be followed by the production of humoral antibodies. There is also evidence that cell-mediated immune responses occur. Peripheral blood lymphocytes of patients partially immune to infection with **P. falciparum** were found to transform into blast cells when incubated with extracts of **P. falciparum** gametocytes or trophozoites, whereas lymphocytes from uninfected persons did not. The ability to transform persisted for as long as two years after radical cure. Chronic infection is associated with gross hyperplasia of the mononuclear phagocytic system. In infected patients, splenectomy is followed by a marked increase in blood parasite levels, but the immunological basis (if any) of this effect is not known. An important role for humoral antibodies in resistance to human malaria parasite is suggested by the beneficial effects of the transfusion of antibody containing serum in infected patients".

Life cycle of malarial parasites: Before active immunization against malaria is discussed it is necessary to be well acquainted with the principal phases of the life cycle of malarial parasites. Large number of sporozoites, the infective stage, accumulate in the salivary glands of infected mosquitoes. During feeding these are introduced in the host which pass into the parenchymatous cells of host liver. This stage is known as primary exo-erythrocytic or tissue stage. Here the parasite nucleus divides many times and cells containing the dividing parasites or exo-erythrocytic schizonts become considerably enlarged. In about 8 days time these rupture and thousands of merozoites are liberated. These merozoites penetrate erythrocytes and depending on species may re-infect other liver cells producing secondary exo-erythrocytic stages. Once within the erythrocytes the parasites digest red cell contents and grow rapidly to occupy much of the host cell. As end products of digestion of host-cell-haemoglobin malarial pigments are produced. Parasite nucleus divides and gives rise to 8 or 16 daughter merozoites in each schizont. The red cells rupture and merozoites are released to infect more erythrocytes. For the purpose of propagation some of the merozoites on penetrating into erythrocytes develop into male and female gametocytes. When these erythrocytes are taken in by mosquitoes further development into male and female gametes take place and fertilization occur. The ookinetes or 'wandering vermicules' thus formed penetrate the mosquito stomach wall and encyst on the outer surface which ultimately give rise to oocysts containing large number of uninucleate, elongate bodies known as sporozoites. When mature oocysts rupture these are released into the haemoceal of the mosquitoes and ultimately reach the salivary glands. The cycle is thus repeated.

Antigens of malarial parasite: From what has been said just now it would be apparent that each stage in the life cycle of malarial parasite differs from the others. Consequently their immunogenicity differ. As a result immunity produced against malaria is not only species-specific but stage-specific also. Moreover intracellular habitat has complicated studies on malaria parasite. It is not known to what extent host recognises parasitized cells rather than parasites alone. Little is known about the immunogenicity of the antigens. Various techniques used to detect and characterise parasitic antigens have shown that these are not necessarily localised in parasites only. Ward and Cornan (1966) have found antigens (1) on the surface of the parasitized cell (at different stage of development), (2) circulating in the plasma of infected individuals, and (3) in association with various organ tissues. There is evidence also that there are common antigens to many stages of parasite life cycle. Collection of required amount of parasitic material for immunological studies has always remained a practical problem.

Sporozoites: These can be obtained by dissecting salivary glands of infected mosquitoes. The other alternative is to remove the developing oocysts by dissecting infected mosquitoes and to culture them **in vitro**. Whichever technique is used the yield is very small. Sporozoites have been used for serodiagnosis and immunisation but so far no detailed antigenic analysis has been made.

Exo-erythrocytic schizonts: This is the most difficult stage to collect in quantity necessary for immunogenicity studies. Preliminary attempts to separate pre-erythrocytic schizonts from sporozoite induced heavily infected mouse liver have been made by **Williamson et al.** Liver parenchymal cells have been cultured **in vitro** and shown multiplication. These are suitable for development of pre-erythrocytic schizonts **in vitro.**

Erythrocytic stages: Of all the stages in the life cycle of malarial parasite erythrocytic stages are easiest to obtain and infected blood remains the most convenient source. Infected blood is collected in anticoagulants and following procedure adopted to separate parasitized cells and parasites therefrom.

(i) **Selective separation of parasitised cells:** Infected erythrocytes are lighter than uninfected ones and on centrifugation lie just under the buffy coat. For selective separation one of the following techniques is used:

(a) Dextran sedimation technique (Spira and Zuckerman 1966).

(b) Low speed centrifugation in sucrose gradient (Williamson and Cover 1966; Williamson 1967).

(c) Millipore filtration technique (Corradetti **et al** 1964; Brown 1966)

(ii) **Release of parasites from infected erythrocytes:** Several methods are available for disruption of infected red cells but contamination with host material cannot be avoided.

(a) **Hypotonic lysis** with distilled water. This is the , easiest technique but it can adversely affect the parasite making them unsuitable for metabolic studies.

(b) **Saponin lysis** (Zuckerman and Ristic 1968 and Williamson 1967). This is a very simple technique but is unsuitable for avian, reticulocyte-preferring **P. berghei** and suspensions containing excess leucocytes.

(c) **Immune lysis:** Immune lysis with anti-erythrocytic serum is a very effective method of lysis but it involves introduction of additional protein.

(d) **Selective disruption of infected erythrocytes in a pressure cell.** (D' Antonio **et al** 1966). It should be conducted carefully to avoid parasite damage.

It would thus be seen that depending on availability, both as regards quantity and ease of procurement, and utility two stages stand out for use as potential antigens for vaccines. Both these are asexual stages, the sporozoites and erythrocytic schizonts and merozoites.

Vaccines

Sporozoites : A vaccine specially protecting against the sporozoite stage is certainly the best for attacking the parasite at the very moment of entrance into the human body. If immunity can be developed against this stage the infection can be cut short at the earliest with least damage to the host. In other words it would be the real causal prophylaxis.

Irradiated sporozoites have been used by many workers for production of immunity and encouraging results obtained. Nussenzweig and her colleagues (1967) observed that x-irradiated sporozoites of **P. berghei** inactivated the parasites and as a result when infected with these no patent parasaetimia was detected. A large percentage of vaccinated mice were protected against injection of viable sporozoites. But this protection was ineffective against blood stages. Clyde **et al** (1973a) carried out similar studies in human volunteers with **P. falciparum.** They irradiated infected mosquitoes carrying sporozoites. These mosquitoes when fed on volunteers, they (the volunteers) became positive for circumsporozoite precipitate (CSP) and when challenged by feeding non-irradiated infected mosquitoes on them, no parasitaemia developed. Further studies with one of the volunteers showed that he was susceptible to strain specific falciparum malaria induced by direct blood transfusion. Further studies by Clyde **et al** (1973b) showed that protection provided by x-irradiated sporozoites of Burma strain of **P. falciparum** was effective against Malaya, Panama and Phillippine strains also but was ineffective against **P. vivax** sporozoites. CSP test was positive not only against Burma strain of **P. falciparum** but against Malaya, Panama and Solomon Island strains also. It was negative against **P. vivax** sporozoites.

Spitalny and Nussenzweig (1973) while working with **P. berghei** observed that no correlation exists between CSP levels and protective immunity although CSP test could be used to measure the immunogenicity of a batch of sporozoites.

Erythrocytic stages and merozoites : Most of the work in this field has been conducted in rodent malaria. Weiss (1965) and Weiss and Zuckerman (1968) observed that a strain of **P. berghei** which became avirulent in mice conferred active immunity in mice against the parent virulent **P. berghei** strain. Multiple injection of irradiated **P. berghei** parasites in recipient rats conferred immunity against subsequent challenge infection with non-irradiated parasites (Wellde and Sadun 1967). **P. chabaudi** (mild chronic) has been found to confer immunity in mice against **P. vinckei** (virulent, fatal) but not against **P. berghei** (Yoeli, 1966; Nussenzweig **et al** 1966).

Early attempts to immunise monkeys with **P. knowlesi** antigen without the use of adjuvants were unsuccessful (Eaton and Coggeshall, 1939; Short and Menon, 1940) though malarial antibodies were found (Eaton and Coggeshall 1939 and Ray **et al** 1947). But monkeys immunised subcutaneously with 2 doses of formalised **P. knowlesi**—parasitized blood emulsified with complete Freund's adjuvant—were extremely resistant to a normally lethal challenge (Freund **et al** 1945, 1948). K. N. Brown (1968, 1969) observed that monkeys immunised with dead **P. knowlesi** schizont-infected cells in 'incomplete' Freunds adjuvant to show only variant specific immune response. In contrast monkeys immunised with parasites with "complete adjuvant" showed prolonged latent period with elimination of parasites from blood. Owl monkeys similarly vaccinated with **P. falciparum** developed infection more slowly than controls (Volter and Rechards, 1968).

Schenkel **et al** (1973) vaccinated Rhesus monkeys with a nonviable antigen given in combination with Freund's adjuvant. It protected the monkeys against a normally lethal challenge of **P. knowlesi.** Use of this antigen alone or in combination with other adjuvant was not successful. The merozoite vaccine developed by Mitchell **et al** (1974) was effective against erythrocytic stages of homologous or heterologous normally lethal **P. knowlesi** parasite. Vaccinated animals once challenged are also resistant to subsequent infection with other variants or a different laboratory strains of **P. knowlesi.** They observed that merozoite vaccination induces immunity far greater in degree and significantly broader in specificity.

Conclusion

From the foregoing discussions two facts would crystallise out. First that immunity against malaria being species-specific, for practical solution to the problem of malaria vaccine, one shall have to concentrate on human malarial species only.

And for this we must have an animal host wherein these can be transmitted through mosquito vectors. The only animal species susceptible to human malarial parasites available to-day is the **Aortus trivirgatus**, the South American Owl monkey. It is in short supply and we in India do not have access to it so far. All the old world monkeys are immune to the human species. Consequently attempts should be made to find alternative animal species to host human malarial species. Meanwhile a few Owl monkeys should be imported to establish a colony for supply to the Indian Scientists. Secondly, as malarial immunity is stage-specific attempts should be made to culture the merozoite and sporozoite stages of the human malarial parasites **in vitro** in sufficient quantities for use in a vaccine. As for merozoites considerable progress has been made towards this goal. But with sporozoites the outlook is rather bleak, as in nature the sporozoite cycle is a self-limiting one and cannot be expected to propagate continuously **in vitro**. It would be necessary to isolate and identify 'the antigens from sporozoites responsible for sporozoite-induced immunity' and synthesize them chemically.

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Immunoprophylaxis against Malaria

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Introduction

Immunoprophylaxis against malaria is a topical problem in the context of the current resurgence of human malaria. Immunoprophylaxis is complicated by the multiplicity of the variants and the phase-specific antigens of the same strain. Attempts are being made in different laboratories to select a phase specific vaccine which would be effective in natural infections.

This paper is concerned with the working out of a potential antigen from infected blood, liver and spleen and the efforts are to use them as immunoprophylactic agents either alone or coupled to immunogenic carriers with or without adjuvants. The purity of these antigens has been established by biochemical and immunochemical methods. The protective effect of these pure antigens have been observed, when mice and rats were immunized with these antigens and were challenged with malarial parasites. The protection achieved is quite promising and it appears that at least immunization with these antigens from blood cells and liver is possible and these could be used as potential antigens for malaria vaccine preparation. Some of the physico-chemical properties of these antigens from different sources were studied and so far, it appears that they are different. The profile of these antigens during the course of infection and recovery is also interesting and is peculiar to each antigen.

Besides, the use of these antigens for immunization purposes, the availability of pure malaria antigen is a prerequisite for a sensitive and specific serological test. With such antigens, tests can be standardized and reference reagents made available.

Material and Methods

Distribution of antigen and antibody specific to Malaria (P. berghei) during the course of infection : The experimental model was rats infected with one million parasites of strain **P.berghei.** Parasite count of the inoculated rats was done everyday by taking the blood from the tail vein. Smears were stained and parasite count made by conventional methods. During the course of infection, at intervals of one or two days, few rats from the infected batch were sacrificed after slight anaesthesia with ether. They were bled from the heart. The blood was collected in O. 15 M sodium citrate in the proportion of one part citrate to 5 parts blood and mixed gently to avoid clotting and hemolysis. All the operations were carried out in cold with containers in chilled melting ice. The spleen and the liver were also removed and after washing and perfusion of liver with saline were stored at -20°C until further use. The blood was centrifuged in cold at 3000 r.p.m. to harvest the plasma which was stored at -20°C until further use as a source of extra cellular free antigen. The cell pack was collected and washed several times with physiological saline and the washed cells were lysed with distilled water. The cell lysate was used as the source of intracellular antigen and was further processed for the purification of antigen, as will be discussed later in the text. The plasma collected at extreme latent stage after repeated challenge was used as "immune serum".

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Detection of malaria antigen and antibody: Large number of rats were inoculated as described earlier. Blood was collected for cell lysate and plasma as described earlier. The cell lysate was treated as the source of crude antigen and the plasma obtained at the recovery phase as the source of antibody. The plasma at the parasitemic period was saved to use it as a source of (free circulating extracellular antigen). The method of detection is counter-electrophoresis using homologous adsorbed immune serum. The antigen and antibody were qualitatively detected by this method but for quantitative measurement, the indirect hemagglutination and reverse passive hemagglutination tests were done. From the experiments, it appears that the free antigen in plasma starts appearing from the 3-5th day and the antibody also starts appearing from the same period. Attempts have been made to quantitate the antigen and the antibody at different stages of infection.

Determination of electrophoresis

(i) **Counter Electrophoresis (CEP):** The method is same as described for the detection of Australia antigen (Gocke and Home 1970). In order to check the antigenic activity during different steps of purification, counter electrophoresis was done using veronal buffer of ionic strength 0.05 pH 8.6. Microscopic slides pre-coated with 0.2 per cent agar in veronal buffer were layered with 2.5 ml of one per cent buffered agar. The electrophoresis was performed at 7.5 mAmp per slide for one h. At the end of electrophoresis slides were washed in saline followed bv washing with distilled water. Slides were dried in air with a layer of moist filter paper covered on the slides. They were then stained with 0.5 per cent of Amido Schwartz Solution for 10 min. and then excess dye was destained with the same solvent.

(ii) **Zone Electrophoresis:** The purity of antigen was checked by zone electrophoresis in agarose with slight modification (1968). All the conditions were similar as in counter electrophoresis except that one per cent agar was replaced by 0.8 per cent agarose and that the electrophoresis was performed for one-and-a-half hours. After electrophoresis, protein was fixed by dipping the slide in picric acid-glacial acetic acid solution for ten minutes followed by staining and destaining of the slides (1968).

Determination of (Indirect) Hemagglutination and reverse passive hemagglutination test: The method of (Meuwissen 1974) was adapted. Indirect hemagglutination test was performed by coating the sheep red blood cells (SRBC) with tannic acid (1/20,000) and then coating with the antigen. The homologous immune serum was used as the source of antibody after adsorption with SRBC. After titration, an optimum dilution (1/10) of antigen was used to coat on SRBC. Doubling dilutions of sera were taken on microtitre plates using microdilutors. The end point was taken where the agglutination was sharply well defined. This was used for the quantitative detection of antibody.

Reverse passive hemagglutination was performed by coating the sheep red blood cells with antibody and for this 1/64 dilution of immune serum gave the most optimum concentration. In this case doubling dilutions of antigen were taken followed by which, antibody coated cells were added.

Purification of antigen from blood: Packed cells from the peak parasitemic period of infected rats were individually washed several times with large amount of physiological saline to get rid of residual plasma from the cell mileu. The cells were lysed with double distilled water individually. Cell lysates centrifuged in cold at 3000 r.p.m to make it clear from stroma and cell debris.

The clear lysates from all animal cells were pooled and precipitated with different concentrations of ammonium sulphate ranging from 20-100 per cent saturation. The activities in all the fractions were checked by counter electrophoresis and immunehemagglutination. It was found that the activity of antigen was present only in 40 per cent saturation of ammonium sulphate as detected by our methods of testing. This material is a source of crude antigen, and was subsequently referred to, in this laboratory, as C40 antigen as obtained from cells at 40 per cent saturation of ammonium sulphate.

It is also observed that the material, crude or purified, is labile at room temperature so efforts were made to make all experiments in cold. C40 antigen was dialysed against chilled distilled water in cold with repeated changes, then finally charged with the starting buffer to be used on DEAE-cellulose column.

The material was chromatographed on DEAE-cellulose by using a series of stepwise buffer gradients with increasing salt concentration and decreasing pH. The buffers used were sodium phosphate 0.015 M, pH 6.3, 0.04 M, pH 6.0, 0.10 M, pH 5.8, 0.3 M, pH 5.5, 0.4M containing 2 M Nacl, pH 4.3. Fractions were collected and were read at 280 nm in an ultraviolet-spectro-photometer. The protein peaks were concentrated and each peak was tested for its antigenic reactivity by counter electrophoresis and by reverse passive hemagglutination.

Method for the preparation of liver and spleen antigens : Liver and spleen from various stages of infection were collected and homogenized in a tissue grinder at 0-4°C. The crude residue was discarded after light centrifugation and the supernatant was precipitated with different saturations of ammonium sulphate ranging from 20-100 per cent saturation. Each fraction was dialysed against normal saline and tested for antigenic reactivity by the above methods. The activity was found in 20 to 40 per cent in case of liver and 60 to 80 per cent in the case of spleen.

These fractions were subsequently referred to, in this laboratory, as L20,L40 antigens, fractionated from liver at 20 to 40 per cent saturation of ammonium sulphate. The fractions from spleen were referred to as S60 and S80 antigens obtained at 60 to 80 per cent saturation of ammonium sulphate.

These partially purified materials were further processed on DEAE-cellulose in an attempt to get purified antigens which could be used for immunization purposes as well as for serological testing.

Determination of Molecular Weight : Molecular weight of C 40-A and L20-A pure antigens were determined on Sephadex G-200 column, using marker proteins by the method of Andrews (1970). The data on elution profile were analysed in the light of the theoritical treatments of gel filtration.

Immunization with C 40-A antigen : Large number of rats in five batches were taken. C 40-A antigen was injected intramuscularly on zero day to one group. Second group was treated as control and was injected same amount of material, obtained from normal rats. The adjuvant selected was aluminium hydroxide gel (soluble adjuvant) and was used in equal volumes with C 40-A antigen as well as with normal material. The immunization schedule was in small doses divided into primary and secondary injections. The third and fourth groups of animals were injected C 40-A antigen and normal material without adjuvant but given exactly same dose intramuscularly on the same days. The fifth group was another set of control which was not injected anything.

After about three weeks of immunization, all the groups were challenged with one million parasites. The parasite counts during course of infection were followed each day.

Immunization with Liver antigen (L 20-A) : From the previous experiments on rats injected with C 40-A antigen, it was thought to try the series in both rats and mice for L 20 purified antigen and also to increase the dose as well as the schedule of immunization up to tertiary injections. The material used was chromatographically pure liver antigen.

Two groups of rats and mice with their parallel controls were taken. The experimental group was injected with L 20-A antigen mixed in equal volumes with aluminium hydroxide adjuvant, intramuscularly for primary and secondary injections. The tertiary injection was plain L 20-A without adjuvant.

After the series of primary, secondary and tertiary injections, the animals were challenged with one-two million parasites and the course of infection followed in control and immunized groups.

Results and Discussion

Attempts regarding immunization against malaria started several decades ago (Cohen **et al** 1961; Margaret 1968; Nussenzweig **et al** 1969, and 1970). It waned off for some time due to the spectacular progress in the development of insecticides and antimalarial drugs. Today that interest has revived, partly because knowledge concerning immune mechanisms in malaria has increased greatly and partly because a need for new methods of malaria control more suited to the requirements of developing countries, has been recognised.

Living vaccines have generally comprised irradiated preparations of sporozoites or asexual blood forms, although attenuated blood forms have also been prepared and used. Dead vaccines have usually employed intact asexual parasites or fractions of these and have been administered alone and in conjunction with adjuvants. Results have shown that both sporozoites and blood form vaccines can confer effective protective immunity. In each case the immunity is phase - specific; immunity stimulated by sporozoite vaccines does not protect against challenge with blood forms, while that induced by vaccines of blood forms does not inhibit the development of pre-erythrocytic forms following challenge with sporozoites.

These investigations have clearly indicated that vaccination against malaria is possible. They have also shown the formidable obstacles that oppose securing supplies of both sporozoites and asexual blood forms in large amounts. It seems probable that the feasibility of vaccinating man against malaria will be demonstrated in the near future. The demonstration that vaccination represents a practical and effective method of malaria control, however, will take much longer.

However, a prerequisite of a sensitive and specific serological test is the availability of purified antigens. With such antigens, tests can be standardized and reference reagents made available. As far as malaria is concerned, no such antigens has been isolated so far, except the one described in this paper.

Keeping these facts in view, as well as reports in literature (Golenser et al 1975), attempts are being made to isolate the antigens from plasma, cells, liver and spleen at different stages of infection; and to use these antigens individually or mixed with each other for immunization purposes. The antigen from cells was isolated at the peak parasitemic period because from the studies on the appearance of antigen, showed that the antigen in blood starts appearing from the 3rd-5th day and persists much longer and is highest at the peak parasitemic period on days 10-15 after infection. The free antigen circulating in plasma is identified but not yet fractionated (Fig. 1). The profile of antibody in plasma (i. e. circulating antibody) is peculiar,

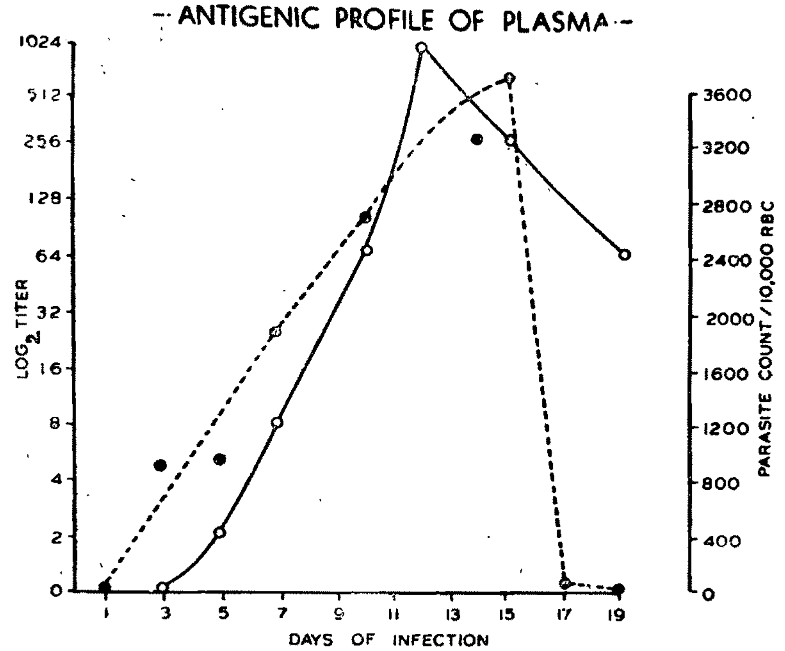

Fig. 1. Status of extracellular, free circulating antigen in plasma during the course of infection. Solid circles indicate parasite count, whereas open circles antigen profile.

as the antigen and antibody in plasma circulate even at the peak parasitemic stage (Fig. 2) and indicate, may be, the same mechanism is operating as in hepatitis-associated antigen and antibody systems.

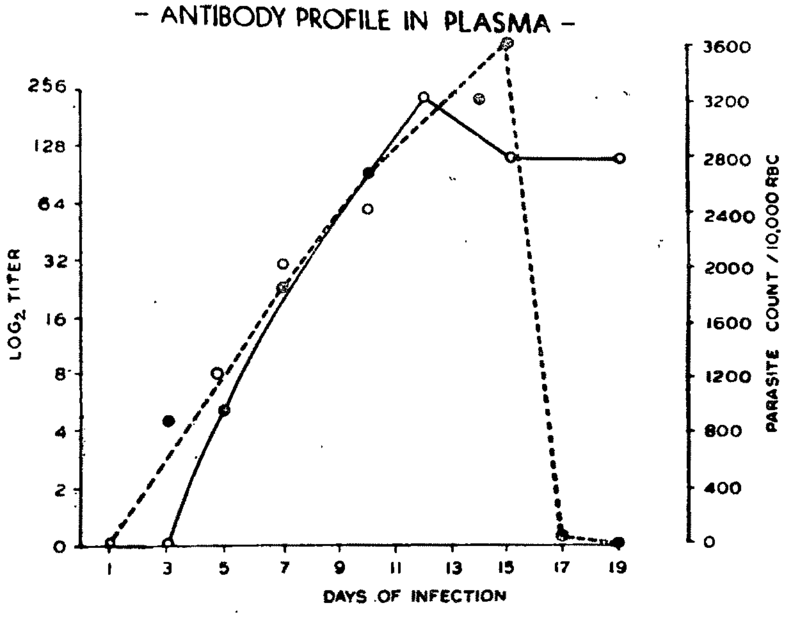

Fig. 2. Status of circulating tin antibody in plasma during the course of infection. Solid circles indicate parasite count, whereas open circles antibody profile.

The elution profile on Sephadex G-75 showed two peaks and the antigenic reactivity was with the first peak, eluting with void volume and there was no antigenic reactivity in second peak. The value of Ve/Vo ratio of the second peak was very much similar to the lone peak of normal cell lysate (Table I, Figs. 3, 4, 5, 6 and 7), indicating thereby the antigenic reactivity and the relevance of the first peak of Sephadex G-75. The precipitation characteristics showed that the antigenic reactivity is in the 40 per cent saturation of ammonium sulphate, hereto referred as C 40 antigen. Further fractionation on DEAE-cellulose with stepwise gradient of increasing salt and decreasing pH, showed that antigen elutes with the first peak at low ionic strength and pH 6.3, giving one band on zone electrophoresis in agarose as compared to crude material (Figs. 8 and 9).

The hydrodynamic parameters and molecular weight of purified blood antigen were determined by gel filtration on Sephadex G-200. The molecular weight is around 45,000 (Fig. 10) which compares well with value of antigen from **P. berghei** obtained by different workers. From the gel filtration data the value of diffusion co-

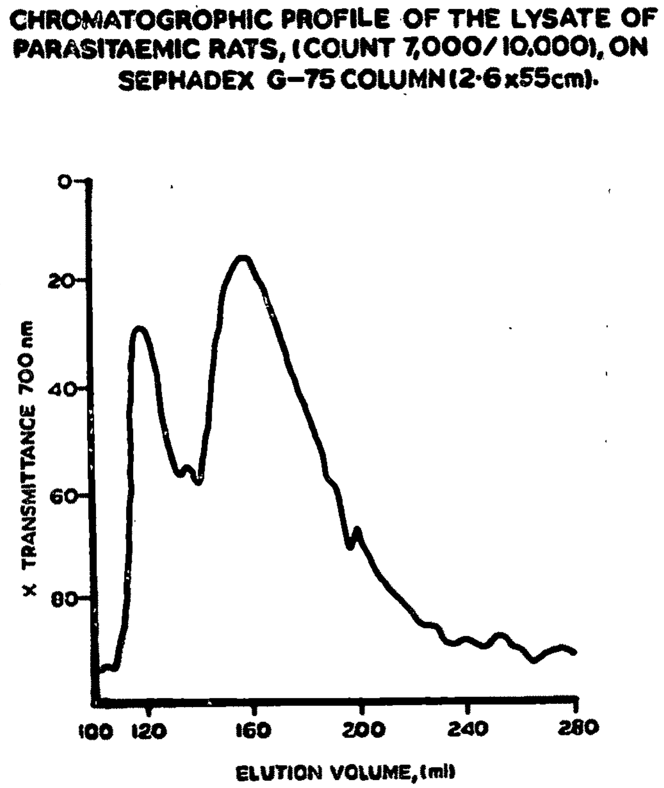

Fig. 3. Blood cell - lysate was fractionated through Sephadex G-75 column. The blood was obtained at peak parasitemic period with count 7000/10,000 RBCs. The first peak is specific to malaria antigen whereas the second peak is non-antigenic.

efficient (D), frictional ratio (f / fo), were found to be 7.9 Cm^2/sec. and 1.25 respectively. These values indicate that purified antigen is a globular and compact protein.

Pure C 40-A antigen was used for immunization of rats and showed the protective effect against malarial infection. The protection was of the order of 60-70 per cent around the period of peak parasitemia (Fig. 11). The antigen from liver was also precipitated at 20 per cent saturation of ammonium sulphate and further chromatographed on DEAE-cellulose column (Fig. 12). The liver seems to have two antigens identified so far, precipitating at 20-40 per cent saturation of ammonium sulphate. The antigen precipitating at 20 per cent saturation of ammonium sulphate (L 20) is present even on the 1st day of infection and stays at higher level until 13-14 day and then goes down slowly by 19th day, when parasite level in blood is also

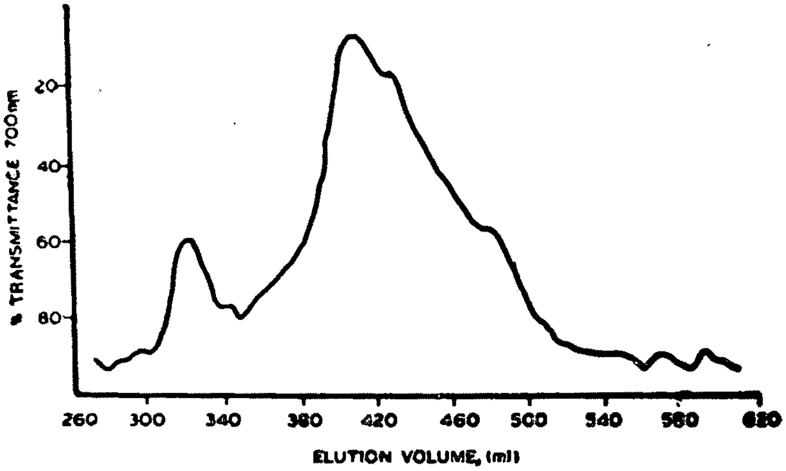

Fig. 4. Profile of G-75 fractionating cell lysate with parasite count 3/10,000 RBCs. The conditions of the experiment being the same as in previous figure. The size of the first peak is smaller, since the antigen concentration is low.

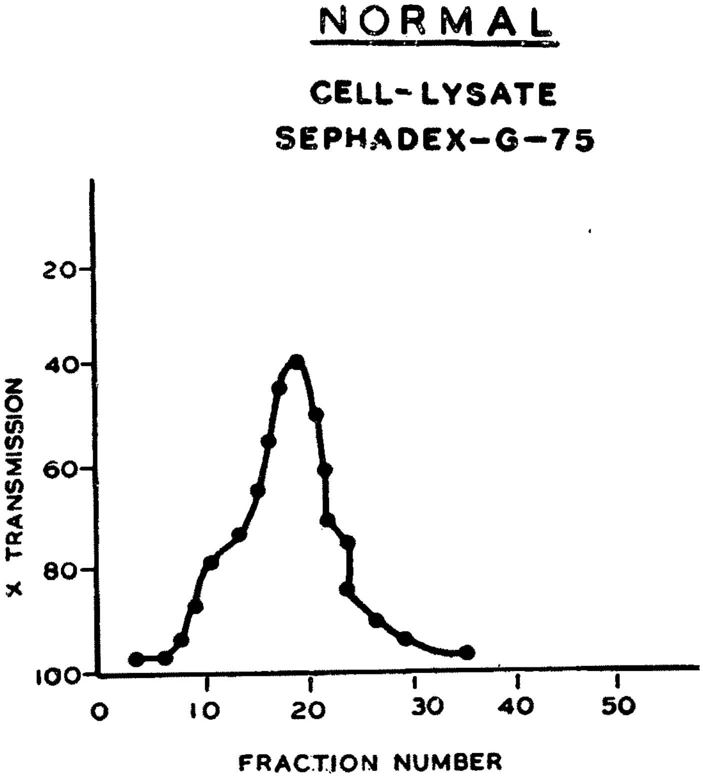

Fig. 5. Profile of normal rat cell lysate fractionated on G-75 column. The peak eluting in this figure corresponds with the non-antigenic peak of the previous two figures.

Ve/Vo Ratio of Sephadex G-75 Peaks of Cell Lysates From Rats with Various Parasite Counts

S. No.	Lysate (count)	Peak	Vo	Ve	Ve/Vo
1	7,000	1st.	124	119	0·96
		2nd.		159	1·30
2	3	1st.	303	320	1·05
		2nd.		408	1·34
3	Normal	1st.	219	280	1·30

Fig. 6. Ratio of elution volume and void volume (Ve/Vo) of the peaks obtained on Sephadex G-75 on fractionation of cell lysates with parasite counts of 7,000, 3 and of normal control.

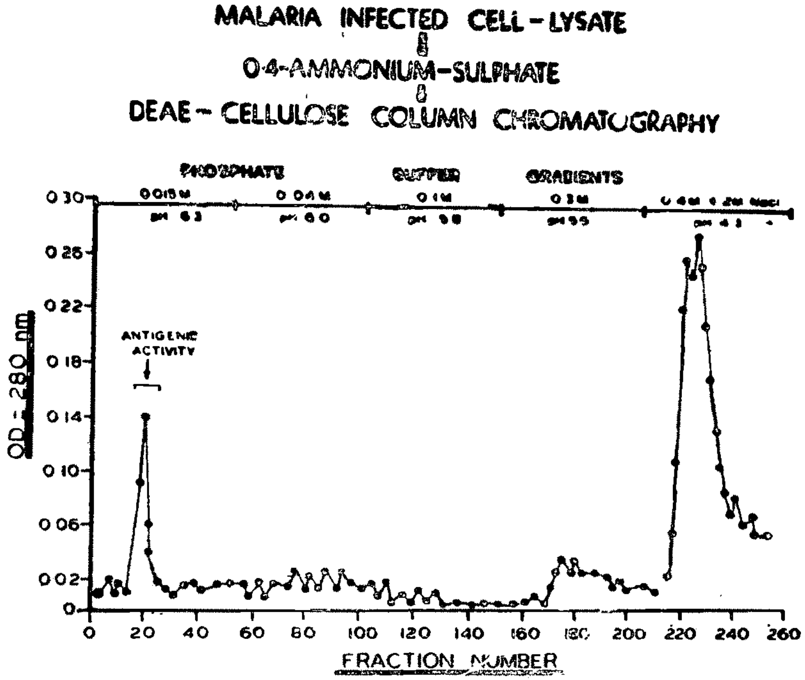

Fig. 7. Purification of (C 40) cellular antigen on DEAE-cellulose column. Stepwise gradients using five buffers of increasing molarity and decreasing pH. The antigenic activity was eluted with first buffer, hence called C 40-A antigen.

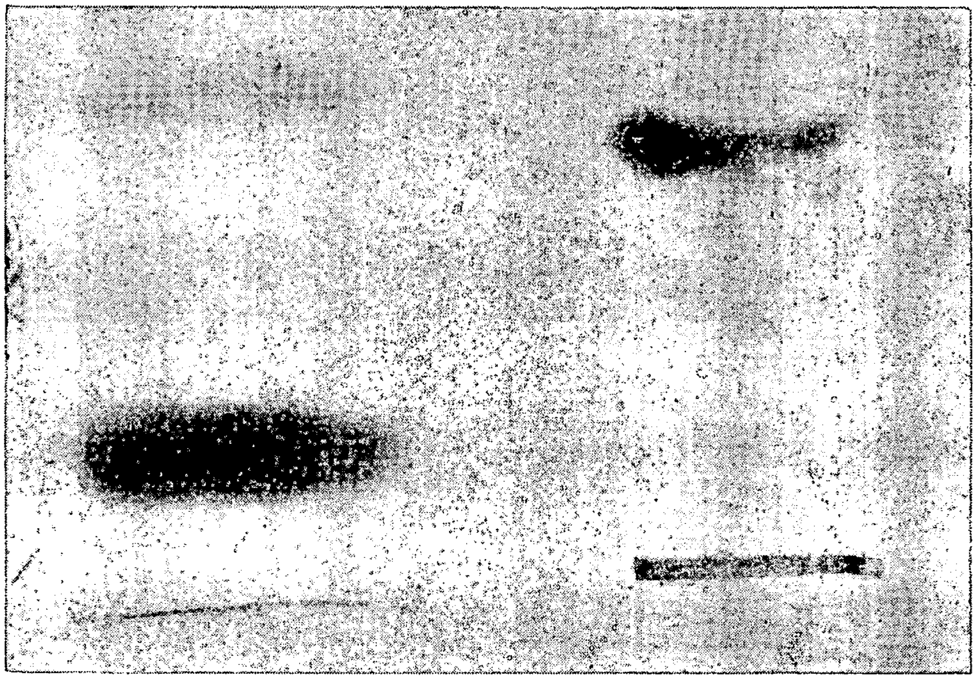

Fig. 8. Zone electrophoresis performed in agarose, using purified C 40-A antigen obtained from DEAE-cellulose column. It shows single band on electrophoresis as compared to crude material. The electrophoresis was performed for one hour at a current of 7.5 mAmp per slide.

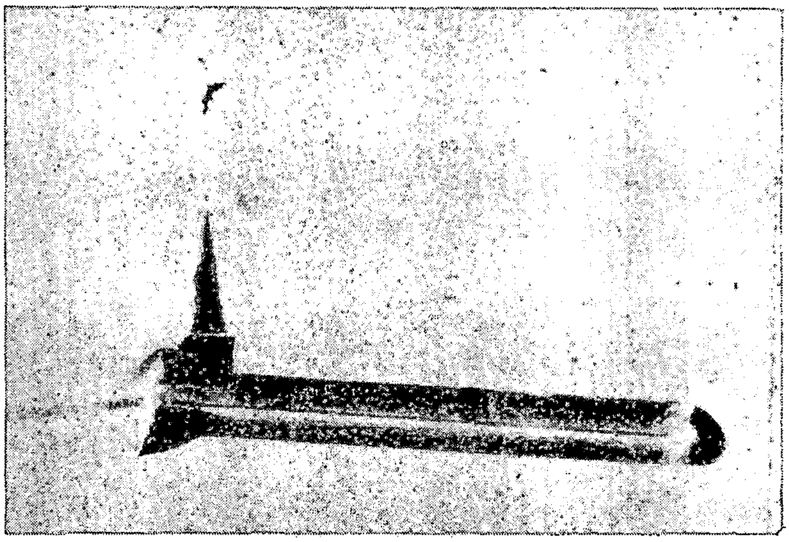

Fig. 9. Disc. electrophoresis of cellular antigen (C 40-A) showing single band.

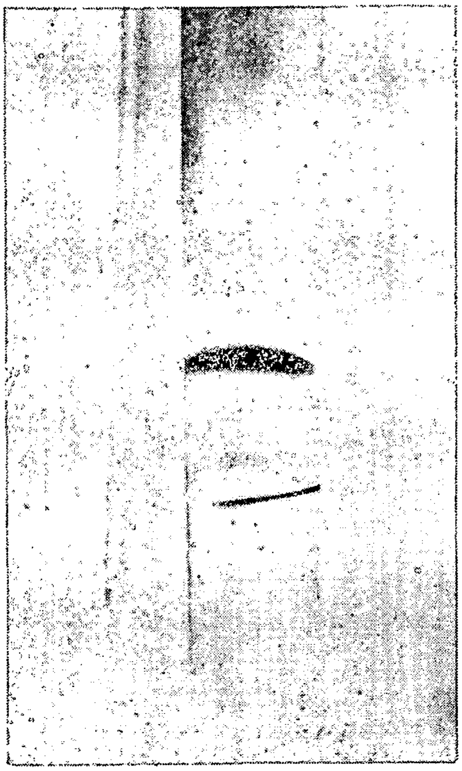

Fig. 17. Disc electrophoresis of pure liver antigen (L 20-A) showing single band.

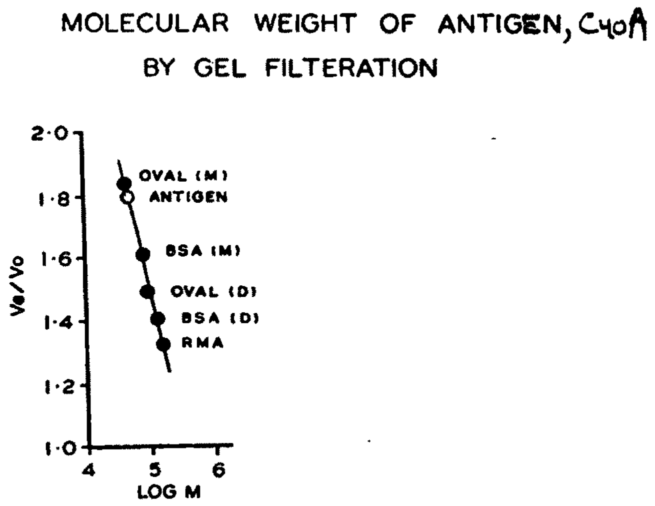

Fig. 10. Determination of molecular weight of pure cellular antigen (C 40-A) on Sephadex G-200 Cclumn.

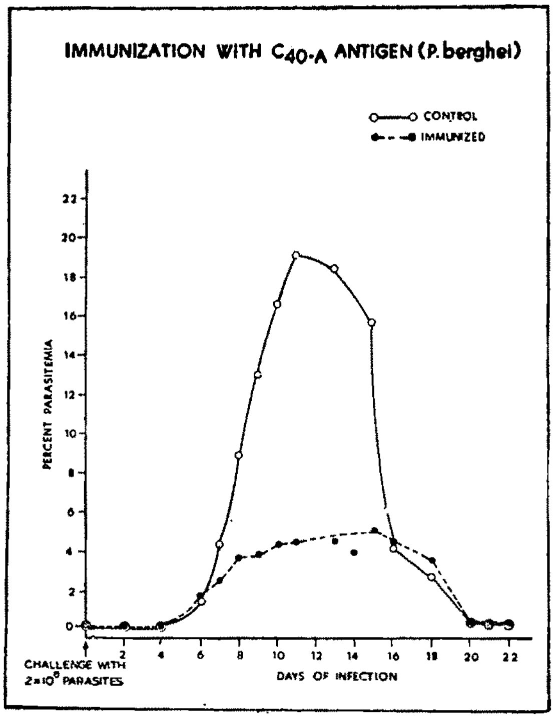

Fig. 11. C 40-A antigen used to immunize rats. Solid circles immunized group and open circles indicate control group.

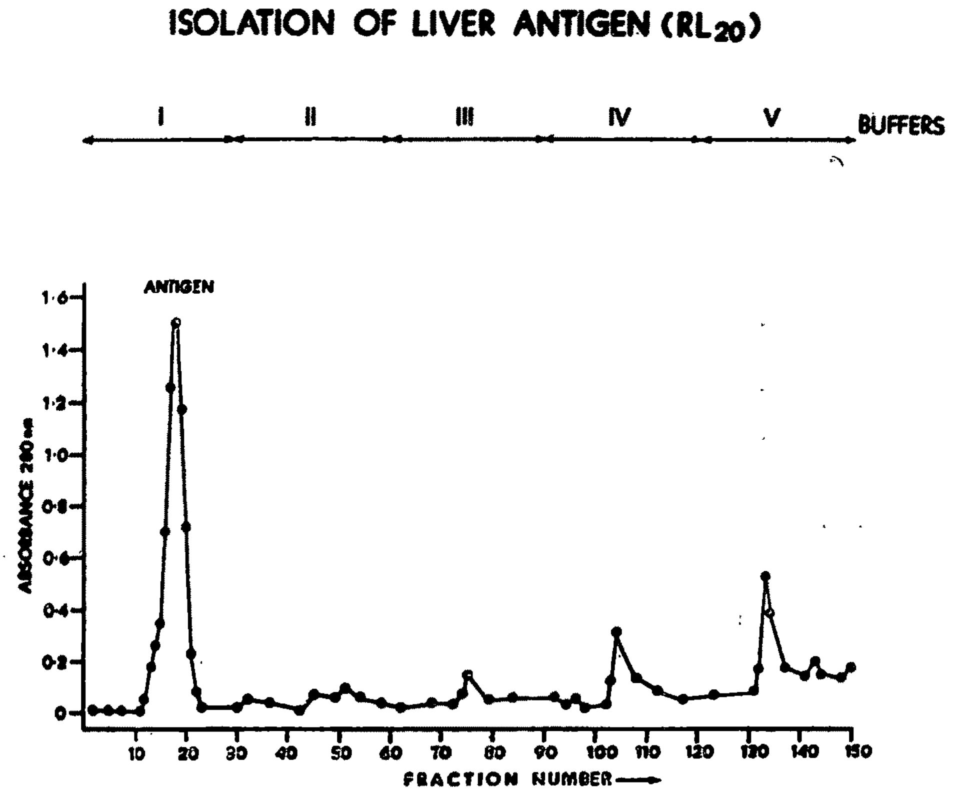

Fig. 12. Purification of (L 20) liver antigen on DEAE-cellulose column. The antigen elutes with first buffer, hence called as L 20-A antigen.

sharply going down. The antigen precipitating at 40 per cent ammonium sulphate saturation (L 40) is slightly different from L 20. This antigen is also present even on 1st day of infection but it gradually increases, with peak of antigenic reactivity on/around 8th day of infection and then stays high even up to 18th day of infection when parasites in blood and L 20 antigen is quite low (Figs. 13 and 14).

Two antigens from spleen have also been identified so far, precipitating at 60 to 80 per cent saturation of ammonium sulphate hereto referred as S 60 and S 80. The appearance of these antigens was also followed during the course of infection as in above experiments. The S 60 is high on the 1st day, and persists high until 13-14 day with peak between 8-9th day and goes down by 18-19th day, along with parasite count. The S 80 antigen is also slightly high on the 1st day but sharply rises and reaches maximum between 8-9th day and stays high even up to 18-19th day when even parasite level is nil in blood (Figs. 15 and 16). Whether the antigen from plasma (P), C 40, L 20, L 40, S 60, and S 80 are same or different antigens and

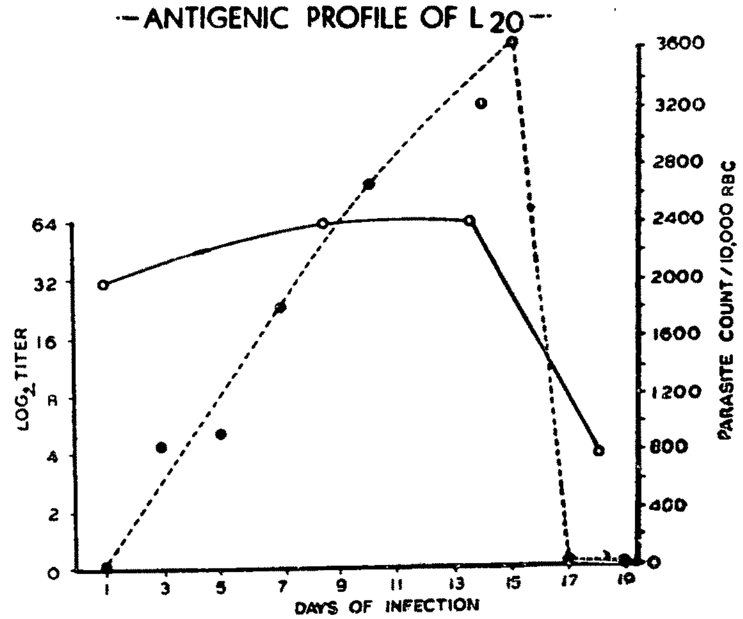

Fig. 13. Profile of L 20 antigen during the course of malarial infection. Solid circles indicate parasite count, and open circles indicate the L 20 antigen.

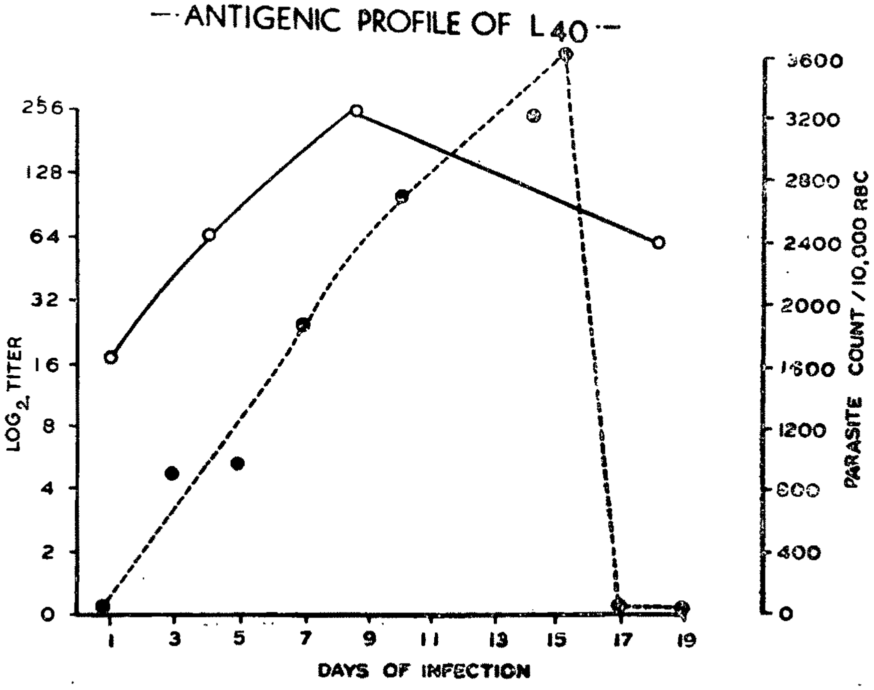

Fig. 14. Profile of L 40 antigen during the course of malarial infection. Solid circles indicate parasite count, and open circles indicate the L 40 antigen.

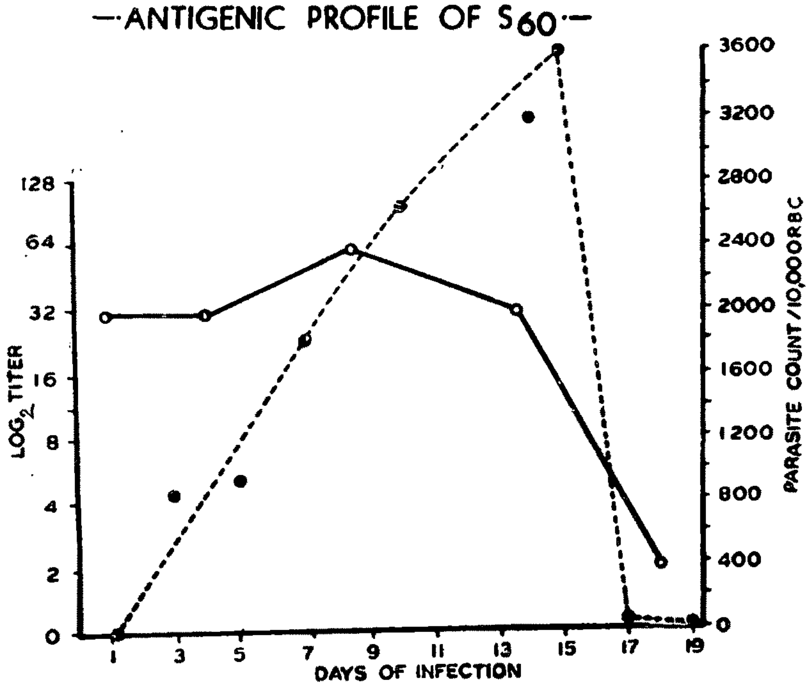

Fig. 15. Profile of S 60 antigen during the course of malarial infection. Solid circles indicate parasite count and open circles indicate S 60 antigen.

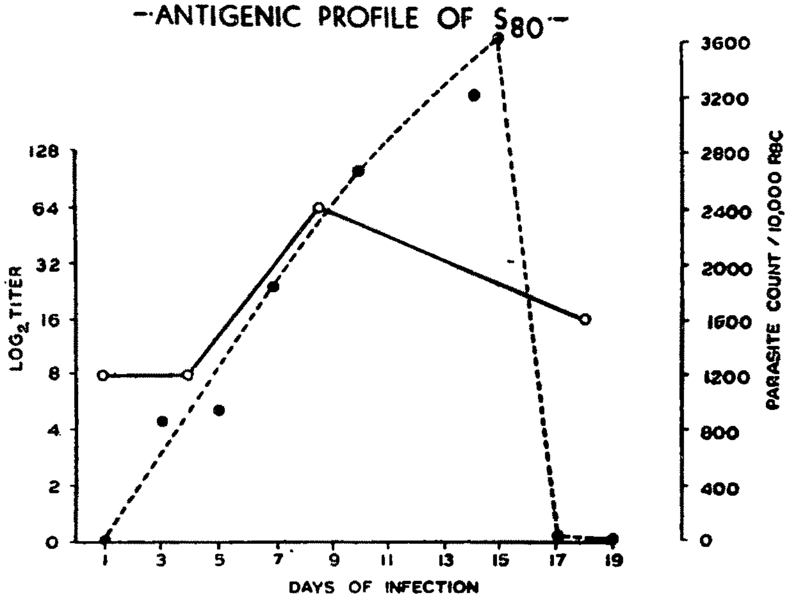

Fig. 16. Profile of S 80 antigen during the course of malarial infection. Solid circles indicate parasite count and open circles indicate antigen.

how they behave as protective antigens either individually or mixed with each other will take time to answer.

The protection achieved with C 40-A antigen is only showing 60-70 per cent effect because the amount of antigen dose used for immunisation is too small and also may be, that the molecular weight of antigen is small, so could be coupled to immunogenic carriers like toxoid, hemocynin etc. and then to be used with adjuvant. The adjuvant selected is good, since this is even acceptable for human use.

Pure liver antigen L 20-A eluting with the first peak of DEAE-cellulose shows single band on polyacrylamide gel electrophoresis and a molecular weight of 12, 590 (Figs. 17 and 18). This L 20-A liver antigen shows 80 per cent protection against malarial infection when immunized with this antigen and control group, were challenged with two million parasites (Fig. 19). This figure depicts that preimmune system

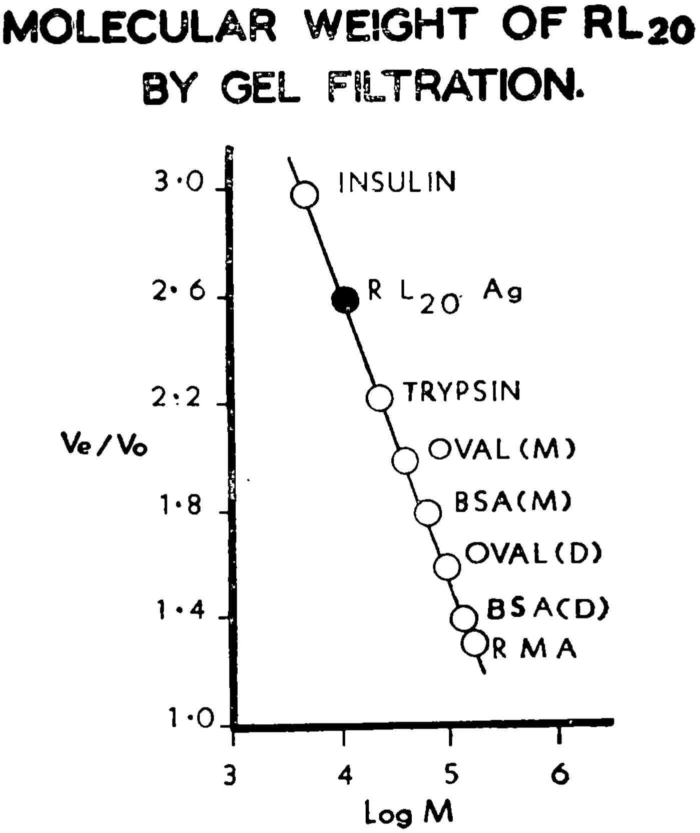

Fig. 18. Determination of Molecular weight of liver antigen, L 20-A.

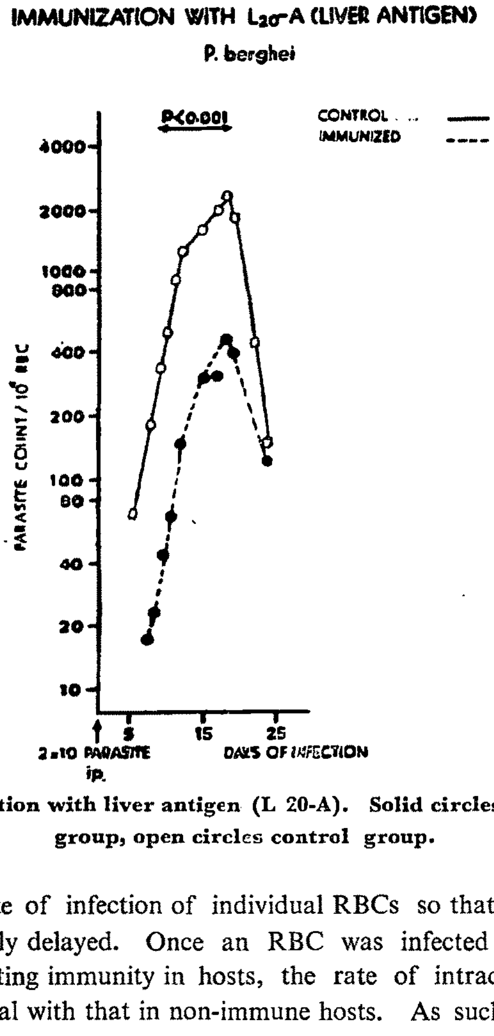

Fig. 19. Immunization with liver antigen (L 20-A). Solid circles show immunized group, open circles control group.

curtailed the initial rate of infection of individual RBCs so that the countable parasitemia was significantly delayed. Once an RBC was infected by a viable parasite, in spite of the pre-existing immunity in hosts, the rate of intracellular multiplication of parasite was identical with that in non-immune hosts. As such, the rate of growth of parasitemia in both cases was comparable, particularly during the log phase of the respective growth curves (16 days in non-immune and 11 days in immune rats). By the 11th day in the immune rats, the experimental infection acted as a booster and the existing immunological memory evidently exacerbated the expression of immune response and that further curtailed the rate of growth in the immune rats after 11th day. This lowering of the rate of growth in immune rats could be due to a severe restriction in the rate of infection through the plethora of humoral immunoglobulins or due to the inhibition of intracellular multiplication or both. In the non-immune series, the natural development of immunity, post infection apparently brought about the same effect after 16 days.

In this system therefore immunisation with tissue phase antigen (liver L 20-A) brought about three effects; (a) Prolongation of incubation period delaying the state of countable parasitemia; (b) Nearly 7-8 times lesser degree of parasitemia than the control; and (c) Due to recall of immunological memory, an early decline of parasitemic phase. It appears that the nature of immunity achieved is of "premunition" type.

In case, such a vaccine is workable in human infection, all three effects will be to a significant benefit to the control programme. Because, through its effect on incubation period the pre-existing immunity through vaccine may bring about a spontaneous cure of natural infection; it may severely restrict the phase of parasitemia and thirdly the low degree of parasitemia which might appear would be controlled quickly.

The experimental tool at hand i.e. immunization with tissue phase antigens has therefore enough potentiality, both applied and fundamental, for a thorough probe and a careful follow-up.

The important aspect of the finding is the liver phase antigen in a blood-borne experimental infection. The nature of the antigen is difficult to speculate at the moment. It may offer several possibilities : (i) the blood parasite partially processed by hepatic tissue was isolated from infected liver. As such, this "hepatic antigen" showed different molecular parameter; and (ii) the "hepatic antigen" might represent a different form of blood parasite persisting in some cells of hepatic architecture. Further investigation would be necessary to exclude the possibility of one or the other.

Acknowledgment

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Studies on Immunization against Experimental Malaria

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IgG class of antibodies of rats hyperimmunised against **P. berghei** infection were able to neutralize completely the infectivity of the organism. The affinity of the binding of the antibody to the parasite is labile to washing. Irradiated parasitized erythrocytes also show promise in inducing effective immunity to that stage. The use of mixed vaccines using irradiated parasitized erythrocytes and sporozoites and identification of merozoite products effective in immunization against the infection are beirg explored in detail.

Introduction

Control of the infected vector and chemotherapy have been the main stay of the National Malaria Eradication Programme which have been used effectively in the control of malaria. However, the recrudescence of malaria in areas believed to be free from the infection resulted in a critical re-examination of the measures so far adopted against the infection. Apart from the logistics such as the inadequate supply of insecticides, factors such as development of insecticide resistance in vectors and drug resistance in the parasite cannot be ignored as contributory factors for this breakdown in the control measures. Under these conditions immunological intervention, if feasible, should be an ideal additional approach in the control and eradication of malaria.

Current status of knowledge on immunization against malaria : During the last two decades much work has been done on the possibility of inducing immunity to malarial infection using different parasitic stages and their antigens. The principal agents used for such immunizations were (1) Parasitized erythrocytes, (2) Sporozoites, (3) Merozoites, and (4) Nonliving parasite antigens.

Parasitized erythrocytes : The effect of immunization of rodents with parasites attenuated by tissue culture passage or by irradiation have been studied by Weiss and De Guisti (1966), Weiss (1968), Wellde and Sadun (1967) and Sadun **et al** (1969). They found significant increase in resistance to challenge in the treated animals. Sadun **et al** (1969) extended these studies to owl monkeys (**Aotus trivirgatus**), using irradiated **P. falciparum** - parasitized erythrocytes. About 50 per cent of the monkeys were protected from the infection by this technique.

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Sporozoites : Nussenzweig **et al** (1969) have been concentrating on sporozoites as these are the first stages that man normally encounters and they found that sporozoites of **P. berghei** when irradiated with 7.5 KR induced protection against malarial infection in the rodents. They further reported that the protection against **berghei yoelii** was extended to **vinckei** strain as well. More recently, these studies have been extended to human volunteers. Rieckmann **et al** (1974) attempted to immunize a volunteer with sporozoites irradiated at 12 KR by allowing the irradiated infected mosquitoes to feed on the person. They found significant protection on challenge with unirriadiated sporozoites. No patent infection was found in the volunteer till 15 weeks after challenge.

Clyde **et al** (1973, 1975) in two separate investigations on humans studied the effect of similar immunization with sporozoites irradiated at 15 KR. In the first study, they observed protection by this procedure in one out of 3 volunteers. In a later study, while they confirmed these findings, it was observed that the protection by this procedure lasted 3 months against **falciparum** and 6 months against **vivax.**

Merozoites : Mitchell **et al** (1975) investigated the effect of immunization of monkeys with merozoites of **P. knowlesi** suspended in Freund complete or incomplete adjuvants. The animals were challenged with immature schizonts. They observed very good protection in the animals with the homologous strain but not with a heterologous **P. cynomolgi bastianelli** strain.

Nonliving parasite antigens : Some attempts have also been made in inducing immunity with nonliving parasite antigens. Zuckermann **et al** (1967) passed **P. berghei** parasites, liberated from infected erythrocytes by saponin, through Hughes Press and used the antigen for immunization of rats. Simpson **et al** (1974) vaccinated 13 monkeys with various nonviable fractionation products derived from **Plasmodium knowlesi.** These were prepared by French Pressure Cell disintegration and differential centrifugation, biogel column separation and linear sucrose density gradient centrifugation. The data of these studies reflected a significant lowering of peak parasitemias of the vaccinated monkeys.

An analysis of the results of these investigations leads one to the following conclusions :

1. In general, these procedures give partial protection. Even with merozoite vaccination of Mitchell **et al** (1975), 3/6 monkeys immunized developed low grade parasitemia.

2. Immunization with one species does not protect against another species.
3. Even within species protection, in general, is variant specific except, possibly with merozoite vaccination.
4. Immunity is stage specific. Immunisation against erythrocyte stages does not protect against sporozoite stage.

The objectives of our study have been to investigate the immunological factors involved in development of resistance in rodents to malaria infection and characterize them. Further, we have been examining the possibilities of inducing resistance using irradiated parasitic stages as immunogens.

Material and Methods

The **P. berghei** (Vinckei and Lips) strain is maintained by serial blood passage in albino rats. Parasitemia was monitored by staining thin blood films by Giemsa or J. S. B. stains. Adult rats weighing about 150 g. each were employed for raising hyperimmune sera. Rats of the susceptible age group (40-70 g. weight) were used for immunization of the animals with irradiated parasitized erythrocytes, and for evaluating the neutralization of infectivity with hyperimmune sera and with fractionated globulins.

Irradiation of the parasitized erythrocytes was done in a Gamma chamber 900 of BARC, Bombay.

For neutralization of the infectivity experiments, one ml. of Krebs-Ringer glucose buffer (KRG), pH 7.4 containing 10^5 parasitized cells was incubated with one ml. of the test serum or 0.3 ml. of globulin with appropriate controls at 37°C for 2 h. The suspension was then injected intraperitoneally into rats. Where necessary, washing was done by centrifuging the incubation mixture at 2000 r.p.m. for 10 min. and resuspending the cells in 2 ml. of KRG buffer which was then injected into the animals.

Results and Discussion

Albino rats exhibit age-related susceptibility to infection with malarial parasite, **P. berghei.** Infection at increasing age results in greater percentage of survival of the animals. Infection at the age of 45 days results in 66 per cent of the animals showing resistance when infected by intraperitoneal injection of 1×10^7 parasitized erythrocytes. When the infection was given at 8 months of age, about 80 per cent of the animals acquire resistance to the infection. In general, the animals on infection develop parasitemia in about 2 days, reach a maximum level in 11 days after which the animals succumb to the infection. In animals that develop resistance to the infection, the parasites disappear from the blood. The animals that develop resistance were taken in the present study. They were hyperimmunized with repeated infections with 10 million parasitized erythrocytes. A total of 9 injections were given each at an interval of 7 days. The animals did not develop infection inspite of such repeated challenges. The sera of these animals was used for the preparation of purified globulins. The globulins were precipitated with 50 per cent $(NH_4)_2SO_4$. These were taken up in phosphate-buffered saline (PBS), pH 7.2, dialysed against PBS and passed through Sephadex G-200 with PBS as eluant. Two peaks were obtained corresponding to IgM and a fraction consisting predominantly of IgG. IgM gave a good indirect hemagglutinating activity but in general IHA titers do not seem to correlate with development of resistance. The fraction under the second peak after lyophilization was again passed through a column of DEAE-Sephadex A-25 and eluted with three phosphate buffers of 0.01 M of pH 7.5; 0.02 M of pH 6.2 and 0.05M of pH 5.5. The peak fraction eluted with 0.01M phosphate buffer of pH 7.5 was pooled and lyophilized. The hyperimmunized serum and the fractions from Sephadex G-200 and that from DEAE-Sephadex A-25 were examined for their protective effect on the infection. The original hyperimmunized serum had a considerable protective effect against the infection. This effect was observed only in rats which received the hyperimmune serum and subsequent washing resulted in loss of protective activity suggesting that the linkage of the antibody to the parasite is labile. The protective effect seems to reside in the IgG fraction as this fraction totally neutralized the infectivity of the parasite on incubation. This was tested by subinoculation of the blood from these animals into susceptible mice which then did not become infected. The antigens responsible for the production of this highly protective antibody is currently under investigation in our laboratory.

It appears from this that humoral antibody alone is effective against malarial infection. While T cell may be involved for the production of the protective antibody, immunity may not be of cell-mediated type involving cytotoxic T cells. However more experiments on T cell role in the infection should be conducted before conclusions are drawn on this aspect.

Studies on immunization with irradiated parasitized erythrocytes : The effect of irradiation of the parasitized erythrocytes on the induction of immunity has been studied. The infectivity of the parasites was not abolished when they were exposed to a radiation dose of 20 KR. However, with 25 KR dose, no development of the parasite was seen from the immunizing dose. There was significant protection (70 per cent) against challenge when animals were vaccinated with 2 doses each with 3×10^8 irradiated parasitized cells at an interval of 7 days. It was observed that the extent of protection increased with the number of vaccinations.

We are currently investigating on the conditions for producing sterile immunity in mice such as the optimal immunizing dose, number of vaccinations and the extent of protection. We are also attempting to raise the sporozoites of this strain for inducing protection in the animals to erythrocyte and sporozoite stages as well.

Studies on merozoite culture : Recent studies of Dennis **et al** (1975) suggests the possibility of cultivating merozoites. The work of Dvorak **et al** (1974) and Miller **et al** (1975) suggests that the merozoite has an anterior end which attaches to specific sites on the erythrocyte membrane. During this process a glycoprotein coat on the surface of the merozoite is pushed back to enable the parasite to penetrate the red cell membrane. Antiserum to the erythrocyte stages seems to inhibit the ability of the merozoite to penetrate the membrane. Attempts are being made in our laboratory to cultivate the merozoites of P. berghei, in large numbers and examine its various antigens.

It would of course be ideal to have a nonliving soluble antigens which is diseffective against malaria. The studies using attenuated living parasites may sometimes have the advantages of nonuniformity of the attenuation.

Acknowledgment

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Development of Newer Drugs against Malaria*

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Introduction

Malaria, a scourge for centuries, seemed to have been conquered but has come back with a vengeance. There were 75 million cases of malaria in 1947 and due to the impact of the National Malaria Eradication Programme, the number of malarial cases was brought down to less than half a million in late sixties. Since then there has been a resurgence of this disease and this year 4 million new cases of malaria are expected. This resurgence of malaria becomes ominous as both the vector and the parasite have developed resistance to insecticides and established antimalaria agents.

The occurrence of drug resistant strains and the absence of an ideal antimalarial drug has enthused a sense of urgency for the search and development of new drugs for malaria. The search for a new antimalarial is replete with problems due to diversity of objectives and needs of the various persons involved in the chemotherapy of malaria. The physician has a need for a new and potent schizonticidal drug or combination of existing drugs that would be effective in patients infected with drug resistant parasites especially, **P. falciparum**. There is an urgent need of new drugs for radical cure of relapsing infections with **P. vivax** and **P. malariae** in order to shorten the time needed for treatment. Such a drug which produces radical cure of relapsing malaria must be highly effective against the exoerythrocytic phase of malaria parasites, **i. e.** against both the primary and secondary tissue phases. Malaria eradication workers need a new antimalarial that can be used for mass drug administration.

A drug that would be more applicable for the needs of malaria eradication programme must be able to break the cycle of transmission from mosquito to man. For this purpose a potent gametocidal or a sprontocidal activity in the drug is needed. Even though a causal prophylactic, acting at the primary tissue stage would also achieve the very same objective, but this mode of action is a less desirable one. With such a drug we would need to treat the total population to protect them from malaria, while a gametocidal or sprontocidal drug would eliminate the risk of infection to the population.

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*Contribution No. 474 from CIBA-GEIGY Research Centre

At the present time we do not have a drug which acts on all the stages of malarial parasite and could be used for the triple objective of providing relief of clinical symptoms, prevent relapses and render patient non-infective to vectors. The ideal drug should fulfil all these objectives and in addition should have the following additional properties: (a) long activity to allow an easy and infrequent administration. Bruce-Chwatt (1967), recommends that an ideal schizonticidal drug should act for 3-6 months after a single dose; (b) capacity for effecting radical cure of **P. vivax** or **P. malariae** infection when given as a single dose or at the most in three day course; (c) should have quick onset of action and provide prolonged protection; (d) should be well tolerated, and (e) should be inexpensive.

A drug with a prolonged action would be especially beneficial for causal prophylaxis of non-immune persons visiting malarious areas, itinerant labourers, nomads and for deployment of army personnel in malarious areas. It would be useful during the consolidation phase of malaria eradication compaigns in problem areas and also during the attack phase in combination with vector control measures.

Principles for the development of chemical compounds : Having established the profile of the new antimalarial, one would need to have the wherewithal to synthesize and evaluate candidate compounds.

There are two possible approaches available for obtaining potential antimalarial compounds. One is the rational and the other empirical. In practice one employs both these approaches; which of the two approaches predominates depends on one's training and background. In antimalarial field both the approaches have yielded positive results. Amongst the rational approach one can consider: (i) Biochemical approaches with the object of synthesising compounds that could selectively interfere with the metabolic process of the parasite, **e. g.** attack on malic and lactic dehydrogenase or search for antipantothenate compounds. (ii) Physiological approach - to synthesise compounds that could interfere with the surface recognition systems of parasites which enable them to identify their preferred location in the body. Malarial parasites are able to recognise the right type of red blood cell and then penetrate into it. Compounds can be envisaged which interfere with this system and can thus blindfold the parasites. (iii) Study of active metabolites of antimalarial drugs. Cycloguanyl pamoate was discovered by this method. (iv) Synthesis of new chemical compounds based on known structure-activity relationship. (v) Analogues of commonly used compounds—the objective would be to look for a more active and/or less toxic compound. (vi) Combination of drugs used in malaria, **e.g.** Pyrimethamine with sulphadiazine. (vii) Compounds used for other diseases, **e.g.** Dapsone or sulphormethoxine.

Empirical approach : This is based on the process of screening a large number of compounds in biological system. This is an expensive procedure as most of the randomly selected compounds are going to be inactive and the probability of coming up with an active compound is low but it has the advantage of bringing up completely novel compounds with probably a novel mechanism of action. Here again one can be selective in the choice of the compounds based on the following criteria : (1) Choose the compounds which have some resemblance to chemical groupings known to have antimalarial activity; (2) Study completely novel compounds; (3) Random sampling on statistically selected basis of all the compounds.

Biological evaluation : Since it is impracticable to first test any new compound in humans, it is necessary to develop alternative procedures of testing **in vitro** or in animal test models. This approach by its very nature is inherently artificial relative to human malaria and may at times give misleading results.

The complexities of malaria chemotherapy both due to variations in drug susceptibility among life cycle stages of malarial parasites and to diversity of objectives, e.g. treatment of acute attack or prophylaxis or interruption of transmission makes the choice of a single test system unsatisfactory and necessitates the use of a battery of tests.

In vitro systems : There is no satisfactory **in vitro** method for assessing antimalarial activity available at present. Cenedella **et al** (1970) have developed an automated technique for measuring the effects of drugs on several metabolic systems. They measure the drug effect on inhibition of glucose consumption, lactate production and release of free amino acids during one hour incubation of **P. berghei** infected rat erythrocytes. The concentration of drugs required to show these effects are much higher than those present **in vivo.**

Canfield **et al** (1970) observed the effects of drugs on morphological maturation of parasites and incorporation of C^{14} methionine into protein and lactic acid production following 18-22 h. **in vitro** incubation of erythrocytes infected with **P. knowlesi.** Chloroquine was shown to be active on all the three parameters studied but other drugs like proguanil, sulphonamides Pyrimethamine and trimethoprim displayed little activity in this test system.

Experimental animal models : A remarkable variety of test procedures are available and these are based on the observation that in addition to man, an unusual range of animals, **e.g.**, lizards, passerine and gallinaceous birds, rodents and the lower primates can act as hosts for Plasmodia.

The experimental models used in malaria research have tended to progressively change as new parasites and hosts became available. In the second and third decades of this century, plasmodial infections of passerine birds were used almost exclusively. The experimental model was based on various modifications of Roehl (1926) procedures using canaries infected with **Plasmodium cathemerium** or **P. relictum.** In late thirties, experimental models based on ducklings or chicks infected with **P. lophurae** or chicks infected with **P. gallinaceum,** were developed. The availability of these models largely replaced passerine bird infections, as they permitted the use of hosts that were cheaper, more readily available and more suitable for various experimental procedures. Concurrently, during the latter half of this period, several simian plasmodia became available. Among these, extensive use was made of **P. knowlesi** and **P. cynomolgi** particularly in Rhesus monkey. During the late 1940s the rodent parasite **P. berghei** became available for experimental use and gained quick acceptance because it permitted for the first time the use of small, cheap and readily available mammal.

Predictability from animal models : It was well recognised that each one of these test systems was deficient with respect to its predictive capability.

This deficiency was offset to a great extent by the ready availability of induced malarial infections in man which could be manipulated quite precisely for pre-field evaluations of agents that had shown promise in one or two of the experimental malarial infections. This accessibility of human volunteers has been curtailed drastically in recent years. Firstly by widespread use of penicillin instead of malaria in the treatment of neurosyphilis; secondly, by changes in the attitudes towards using volunteers for human experimentation, and thirdly by the risk inherent in the use of multidrug resistant parasites in volunteers. This necessitated the development of animal model systems in which infections with human plasmodia may be studied directly.

The investigations of Young and his colleagues (1966) who demonstrated that the Panamian **P. vivax** infection can be transmited in Aotus trivigatus and the success of Geiman and co-worker (1969) in infecting Aotus trivigatus with East African and Malayan strain of **P. falciparum** were extremely timely and are of great interest to chemotherapy of malaria. The demonstration that untreated, intact owl monkey would support highly reproducible infection with a variety of strains of **P. falciparum** and **P. vivax** and that the response to standard antimalarial drugs would simulate the response in volunteers or patients from whom the strains were obtained, has eliminated to a great extent the uncertainties associated with the use of nonhuman malarial parasites and has increased the predictability of the results obtained from such test systems for human treatment.

General principles in selection of test infections in animal models: A battery of test systems have to be used, as it is not possible to rely on any single test for defining the antimalarial activity of the compound. Primary tests in mice and birds serve to define compounds of potential interest. Secondary tests in these animals and lower primates are used for further characterisation of compounds. These tests provide information on such aspects as activity against drug-resistant parasites, effect in a veriety of malarial infections and repository activity.

The primary testing is done in mice infected with **P. berghei.** It has been used extensively for studying the effect on asexual blood forms and recent work gives a basis for studying the effect of drugs in fixed tissue stages of **P. berghei** in mice (Davey. 1963; Yoeli **et al** 1965; Most **et al** 1967; Berberian **et al** 1968). **P. gallinaceum** in chicks is also commonly chosen for primary screening in addition to mice (Davey, 1963). This bird model is suitable for study of both blood forms and tissue stages. It also offers the advantage of an abundant supply of sporozoite and the ease with which mosquitoes can be infected, thus facilitating the transmission of malaria. Another advantage is the freedom from complicating inter-current infection, along with low cost and easy availability. **Plasmodium lophurae** is equally useful for testing against asexual blood form, but not for testing against exoerythrocytic forms as it apparently lacks tissue stages (Reilly **et al** 1949; Thompson **et al** 1953). **P. berghei** is the current infection of choice as it is the only parasite which has been made resistant to all the main types of antimalarial drugs (Thompson **et al** 1967).

The secondary evaluation of drugs can best be done in Simian malarias. **P. knowlesi** infection in rhesus monkey is useful for assessing the effect of drugs on asexual blood forms while **P. cynomolgi** infections in rhesus monkey are useful for evaluating drugs against both asexual blood form and tissue stages.

Finally testing of drugs in owl monkey infected with non-resistant and resistant strains of **P. vivax** and **P. falciparum** would increase the predictability of the test methods. This test model is being intensively used in chemotherapeutic studies (Schmidt, 1973).

Primary test against schizonts : Mice infected with **P. berghei** are treated with the test compound. Blood smears are prepared on the day following the last dose of the drug. Drug effects are assessed by comparing the percentage of cells parasitized in treated and control group (Thompson et al, 1969). The activity of the test compound is compared against quinine, which is used as a reference standard, as it produces about 90 per cent suppression. The tolerability of the test compound is judged from the weight changes and mortality produced at different dose levels used in treating the infected mice.

The rate of parasitaemia developed by **P. berghei** is suppressed by inanition and experience in drug testing has shown that with daily food intake of less than 1.5 g. per mouse it is hazardous to conclude that suppression is due to drug activity (Thompson, 1968). Suppression of **P. knowlesi** parasitaemia in monkeys by inanition has been reported by Geiman and McKee, (1948).

There are some defects in this test model which should be mentioned. The course of parasitaemia varies considerably from mouse to mouse. Secondly, the infection responds poorly to some useful drugs and is hypersensitive to others (Thompson **et al**, 1967). It responds poorly to Chlorguanide because of the limited capacity of mice to metabolise the compound to its active dihydrotriazine metabolite. **P. berghei** is hypersensitive to sulphonamides and sulphones. Thirdly, contamination of **P. berghei** by eperythrozoon coccoides, an ubiquitous natural pathogen of mice greatly reduces the intensity of infection and thus complicates the assessment of chemotherapeutic results (Peters, 1965).

Chicks infected with **P. gallinaceum** infection can also be usefully employed for testing drugs (Davey, 1946 and 1963). The model permits the assessment of short term effects on asexual forms but long term assessment on eradication of blood forms may be complicated by the presence of secondary tissue stages.

P. lophurae infection in chicks have been used extensively and offer the advantage of uniform infection and permits the assessment of drugs on asexual blood forms without the complication of blood parasites arising from tissue stages. **P. lophurae** is not markedly susceptible to sulphonamides and appears otherwise to show relatively good correlation with the action of drugs in man (Reilly **et al**, 1949 Thompson **et al** 1953; McCarthy **et al** 1957; Davey 1946).

P. lophurae infected ducks are not being widely used these days because of the occurrence of delayed deaths after inoculation with parasitised blood evidently due to filterable agent (Dearborn, 1946).

Primary tests for activity against exoerythrocytic form in animals : Sporozoite-induced infection of **P. gallinaceum** in chick is the most extensively used procedure and the drug effects are assayed against the primary exoerythrocytic forms. Aedes aegypti is usually used as the Vector (Davey, 1946, 1963).

Activity against exoerythrocytic forms can be assessed by examining brain smears for tissue forms. Active drugs either prolong survival time or prevent death which occurs due to extensive blockage of the brain capillaries by secondary exoerythrocytic forms. In this test various sulphonamides and chlorguanides are highly effective; Pamaquine is slightly active but quinacrine is inactive even in high doses (Davey, 1963). Such results agree only in part with the known activity of these drugs against tissue stages in man. Hence tests against tissue stages of **P. gallinaceum** while useful may not be entirely adequate in the evaluation of new compounds.

Recent studies enable the use of sporozoite-induced infection of **P. berghei** for evaluating drugs against exoerythrocytic stages (Yoeli **et al** 1965; Most **et al** 1966) Anopheles stephensi is used as a vector and primary exoerythrocytic forms develop during 48-51 h. Overall the **P. berghei** tissue stage test system apprears to be more promising than **P. gallinaceum** system, but the short generation time of primary tissue stages in **P. berghei** is a limitation. It allows little time for drugs that act slowly. Primaquine and possibly pyrimethamine are known to be effective in preventing infection from becoming established but chloroquine, quinine and sulphone DDS were inactive prophylactically (Most **et al** 1967). Recently, procedures have been developed for distinguishing between direct effects on primary tissue stages of **P. berghei** and subsequent action on asexual blood forms due to residual drug. Using this method Primaquine (100 mg./kg.), pyrimethamine (1 mg/kg.), chlorguanide (10 mg./kg.), cycloguanil (100 mg./kg.), dapsone (10 mg./kg.) and sulphadiazine (1 mg./kg.) were found to be active against tissue stages of **P. berghei** but chloroquine (100 mg./kg.), quinacrine (100 mg./kg.) and quinine (300 mg./kg.) were inactive (Gregory and Peters, 1970).

Secondary tests for activity against asexual blood forms in animals : This is done in Simian Host. The principal test infections in the past have been **P. cynomolgi** or **P. knowlesi** in rhesus monkey. During the past few years many strains of human plasmodia, particularly **P. falciparum** and **P. vivax** have been adapted to Owl monkey (Aotus trivigatus) (Young **et al** 1966; Porter and Young, 1967; Geiman **et al**, 1969). Schmidt (1973) has used trophozoite induced infections of **P. vivax** and **P. falciparum** in owl monkeys in his studies on drug resistant malaria.

It is simpler to evaluate the effect of drugs against asexual blood forms with trophozoite induced infections in primates as these do not apparently lead to the development of tissue stages which tend to complicate the assessment.

Schmidt and Genther (1953) have developed procedure for testing drugs against asexual form of **P. cynomolgi.** The performance of standard suppressive antimalarials in this test has given good correlation with their effect in man (Thompson, 1968).

Richardson **et al** (1946) have described procedures for evaluating drugs against **P. knowlesi** induced infection in young rhesus monkeys. **P. knowlesi** responds to standard suppressive antimalarials and is particularly sensitive to sulphonamides. The latter feature does not agree with **P. vivax** infection but agree reasonably well with **P. falciparum** infection in man.

Schmidt (1973) has described procedures for evaluating drugs in owl monkeys infected with **P. vivax** or **P. falciparum.** Treatment is started only after infection has been established and infection density of 20-100 parasites per 10,000 erythrocytes is obtained. The assessment is based on (a) the daily dose required to achieve apparent clearance of an established parasitaemia; (b) dose required to cure established infection. The correlation between responses of antimalarial drugs in owl monkey and man has been good and its predictive value has thus been verified.

Secondary tests for activity against exoerythrocytic forms in animals : The main procedures in current use are based on sporozoite-induced infection of **P. cynomolgi** in rhesus monkeys (Schmidt and Genther, 1953 and Schmidt **et al** 1966). The monkeys are infected intravenously with sporozoites collected from anopheles freeborni mosquitoes. Untreated controls usually develop patent infection within 9-13 days. Prolonged delay of patency or failure to develop a patent infection is indicative of activity against primary tissue stage.

Similar procedures may be used in evaluating effects for radical curative effects with the exception that treatment is delayed until patent infections have developed following sporozoite inoculation.

Primaquine acts as a prophylactic in sporozoite-induced **P. cynomolgi** infections and produces radical cure when given with an effective schizontocide. It thus exhibits activity against all tissue forms. Schmidt (1971) found that chloroquine, quinine, chlorguanide, Pyrimethamine and sulphadiazine were only active against blood forms. **P. cynomolgi** tissue form test system thus gives results that agree quite well with apparent activity of drugs against tissue stages in man.

Procedure for evaluating the activity of drug against malarial parasites in mosquitoes : Mosquitoes are allowed to feed on suitable carriers of gametocytes usually chicks infected with **P. gallinaceum.** The drugs are given in sugar water and effects are assessed on basis of oocyst or sporozoite development.

Procedures for detection of repository activity of a drug : The drug is given prior to infection with the trophozoites of **P. berghei** in mice or **P. cynomolgi** in monkeys. The duration of protection is determined from the time elapsing between administration of the drug and the development of patent infection.

Evaluation of curative action : Dependable procedures for evaluating radical cure action of drugs are : (1) Persistently negative blood smear; (2) Failure of sub-inoculation with blood to induce patent infection in normal test animal; (3) Failure to induce relapse by a provocative procedure as splenectomy; (4) The development of acute infection after re-inoculation with the same strain of parasites as used in the initial infection.

A case for combination therapy : There are many valid reasons for the preferred use of a combination of drugs to combat malarial infection. Thus two drugs may be superior to either drug alone in providing (a) broader activity against various life cycle stages; (b) broader activity against drug resistant parasites; (c) reduced likelihood of acquired resistance, and (d) synergism against asexual blood forms.

Evolution of an antimalarial agent : In principle, the evolution of a new antimalarial agent follows the same pattern as the development of any modern therapeutic agent. Thus, once an interesting antimalarial activity has been observed in the laboratory screening models, the compound is subjected to detailed pharmacological testing to ensure that it does not affect any vital physiological function, e.g., a compound producing profound cardiovascular or CNS effects or effects on other physiological systems would not be suitable for antimalarial therapy.

Once it is established that the compound does not possess an unfavourable pharmacological profile, a thorough investigation of its toxicological profile is initiated. This includes acute toxicity studies by several routes in several species of animals, followed by range finding to assess the dosage that can be used for subacute and chronic toxicity studies. Chronic toxicity studies are conducted in at least 2 species, one rodent usually a rat and the other species being the dog or the monkey. During these chronic toxicity studies, a close watch is kept on the food intake, general behaviour and effect on vital organs by employing special biochemical tests e.g. SGOT, SGPT and other tests like ECG and fundoscopy, **etc.** At the end of the stipulated period of drug administration the animals are sacrificed and various tissues are checked for any histological changes. These tests are designed to determine the organ system most vulnerable to the drug by including a range of dosage extending clearly to the toxic level. In addition, the effect of the compound on reproductive processes is studied. This includes effect on fertility, development of foetus in utero and the effect of the drug on the offsprings.

Drug metabolism : It is important to have information not only on how the drug affects living organisms but also on how the body deals with the drug. The pattern of absorption, excretion and the sojourn of the drug can be determined by using an appropriately labelled compound. This is usually done by using ^{14}C or tritium label. The identification of metabolites is important in order to know whether the metabolite is active or not and also to determine the frequency of drug administration and the dosage regimen.

The discovery of cycloguanil was the outcome of studies on metabolism of chlorguanide. At this stage a cold method for measuring the blood level and steady state levels is developed. This needs the use of sophisticated gas chromatographic and/or high pressure liquid chromatographic techniques. As the selected methodology should be sensitive enough to detect the drug and/or its metabolites in even nonagram quantities, the development of these techniques may take as much as 6 months to one year depending on the nature of the compounds.

Side by side with the development of drug metabolism studies, the pharmaceutical development group is busy developing a proper dosage form, in the peroral form of tablets or a repository intramuscular injectable form.

This type of formulation, especially the particle size is important for the duration of action. Cycloguanil is a good example of this type of development. Cycloguanil hydrochloride was very shortacting and the development of an acceptable Pamoate salt led to the introduction of a repository preparation.

The stage is now set for human clinical trials. First the tolerability and pharmacokinetics are worked out in healthy volunteers. The preliminary drug efficacy studies are best done in volunteers infected with malarial parasites. If the compound still looks interesting then trials in hospitalised patients to assess its efficacy and tolerability are done.

Finally, controlled large-scale trials in hospitals and under field conditions are carried out to establish the place of the new compound in relation to the previously available drugs in the treatment of malaria.

Problems of chemical development have to be tackled before large scale production becomes feasible. This needs special chemical and chemical engineering skills. The odds against development of a new drug are very high and it needs a multidisciplinary team with a great deal of imagination and dedication.

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Chemoprophylaxis in the Control of Leprosy

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Leprosy seems to be on increase in this country in spite of our efforts to contain the disease. Prerequisite to the control of any infectious disease, and particularly leprosy, is a study of three important facets of the disease : (1) man and his reactions to the invading organism, (2) the nature of the invading organism itself and (3) the mechanism of transmission. In case of leprosy, there are several areas, which are beset with our ignorance. It is true that, during the last few years, our knowledge of the various facets of this disease has advanced remarkably, particularly after the introduction of "Mouse foot pad model" for growth of lepra bacilli. However, the mycobacterium cannot yet be grown in a medium satisfactorily. We do not know as yet how the disease is transmitted. There are many leprologists, who believe that the original concept of intimate skin to skin contact may not be the method of transmission. Are arthropods involved in the transmission of the disease ? More recent work by workers from the Jawaharlal Institute for Postgraduate Medical Education and Research, Pondicherry, has raised a possibility of arthropod involvement in the transmission of the disease. There is also a strong suggestion that the disease may be transmitted through inhalation. A large number of bacteria are being shed, particularly in lepromatous leprosy, from nasal secretions as well as from the broken skin.

Advances in the chemotherapy of leprosy have been rather slow. It is true that a few valuable drugs have been added in recent times. With the advent of Shepard's Mouse Foot Pad Model, and more recently, Storr's 9-banded Armadillo Model, it is expected, particularly with the latter, in which the disease can be studied in its entirety, that there will be more satisfactory methods for screening new compounds.

To understand the significance of chemoprophylaxis in a disease like leprosy, one must take into account several factors. Knowledge of distinct epidemiological characteristics of leprosy is a logical prerequisite to the understanding of the role of chemoprophylaxis in the control of leprosy. The number of prevailing cases in a community gives an idea of the endemicity and hence the significance of the importance of chemoprophylaxis.

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*Director

The number of prevailing cases, according to Bechelli **et al.** (1972), in the world is about 10 to 12 million. It is quite disturbing that out of these, almost one-fifth, **i.e.** 3.1 million cases occur in India. In Maharashtra, according to Kapoor (1975), there are about half a million cases, **i.e.** 3.5 to 4 lakh cases, while in Bombay, there are 80,000 patients on the register of the Acworth Leprosy Hospital. The magnitude of the problem of leprosy becomes evident. Prevalence rate is the ratio of the number of cases prevailing in an area at a given point of time divided by the total mid-year population of the area in that year multiplied by 1,000. Estimated on this basis, the prevalence rate in India works out to be 6 per 1000, while in Maharashtra it works out to be 8 per 1000*. According to the W.H.O. Leprosy Epidemiology Team, a correction factor of 300 per cent, **i. e.** three times, is to be applied to the actual prevalence rate. This will raise the prevalence rate in Bombay to the frightening figure of 30 per 1000. From the area-wise distribution of new cases, **i.e.** resident and non-resident cases registered at the Acworth Leprosy Hospital and Greater Bombay Leprosy Scheme Clinics, as reported by Koticha **et al** 1975, it is quite evident that from 1963 to 1972, there is an increasing trend of new cases registered. It is true that some of them are the non-resident and include patients coming from outside Bombay, but there is a definite evidence for increase in the residential cases too. While high incidence rate would mean greater number of active or infectious cases, it may also mean increase in case-detection either as a result of increased surveillance or better awareness among the medical personnel and the lay public. These infectious cases continue to cause anxiety in view of the fact that they are the known source of infection in and about their vicinity.

Is there a high risk of developing leprosy in the contacts? Several studies indicate that the incidence of the disease in those who are in direct contact with infectious cases is decidedly higher. In endemic countries, leprosy is acquired at an early age. There is also a strong evidence that there is a greater childhood susceptibility. It is not known precisely whether continuous contact is more dangerous than repeated contact. In the words of Dr Wardekar: "In the context of our inadequate knowledge about the period that is necessary for transmission to occur it seems safer to use the word 'repeated' instead of 'prolonged contact'." We do not know precisely the role of several factors conducive to high susceptibility. Cochrane, as quoted by Badger (1964), does not believe that nutrition affects occurrence or course of the disease. Other factors which have been implicated are hormonal influence, genetic predisposition, intercurrent infection, tissue temperature and immunologic states of an individual. More recently, the work by Godal **et al** has proved beyond doubt that there is an evidence of sensitisation by the antigen of **Mycobacterium leprae** of the individuals in direct contact with active cases of lepromatous leprosy. This has been studied by the techniques of lymphocyte transformation and leucocyte migration inhibition tests. It is possible, therefore, on the analogy of tuberculosis, that most of us, at some time or the other, must have been infected by **Mycobacterium leprae.** While some develop active disease as a result of combination of factors, others escape due to factors such as high resistance, less genetic predisposition and by mounting up of intensive immunity. Thus, the entire spectrum of events may be: All individuals exposed to infection putting up a high resistance, although sensitized to the mycobacterial antigen, do not show the manifestation of disease, patients of tuberculoid leprosy (T.L.) showing a very positive evidence of high cellular immunity against the disease at one end and the lepromatous type (L.L.) with a near complete lack of immunologic response on the part of the host.

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*According to Koticha, Superintendent, Acworth Leprosy Hospital, Bombay (1975), it will work out in Bombay to be 11 per 1000 on the basis of cases registered at Acworth.

With respect to spread of disease, Meade (1974), has demonstrated a close analogy between viable **Mycobacterium leprae** and **Mycobacterium tuberculosis** in the nose blows and sputum. Meade's work shows bacillary count in the nose blows, single or total nose blows in 24 h., in patients of lepromatous leprosy in comparison with 12 h. sputum output with bacterial count in tuberculosis. An average age and sex specific rate for tuberculosis and leprosy in family contacts in India, as reported by Meade shows that the two are comparable. Figueredo studied 1046 contacts of patients of leprosy and showed that out of 1046 contacts, 291, i.e. 27.8 per cent were infected. In the analysis of the various factors responsible for heavy infection, he found that particularly the young age group was at a very high risk. He further showed that the risk of infection in the contacts of untreated cases is three times as high as in the treated cases.

The problem of contacts in cases like leprosy assumes a great significance because of the fact that it is difficult to establish with precision the duration of contact with a patient of leprosy. This is because of the fact that, by the time, the patient comes with the manifestation of the disease or diagnosed, he may be shedding millions of bacilli from the nasal secretion, and, therefore, infecting his contacts. Thus, it is quite evident that contacts have a high risk of developing leprosy, particularly in the younger age groups.

Screening programme of drugs : Drug screening programme in the preclinical stage in a disease like leprosy has obvious limitations. Firstly, there are no **in vitro** methods to study the antibacterial activity of a drug. The model suggested by Shepard and Rees is certainly valuable, but is expensive, time-consuming and requires careful standardization. It has certain limitations of its own. One must have a very critical inoculum for establishing a good mouse foot pad model. The inoculum usually suggested is 5×10^3 to 1.0×10^4 bacilli per pad. The model is quite sensitive to slight differences in techniques, the temperature and the concentration of the reagents used. Viability of the organisms is on the basis of morphology revealed by the staining characteristics. A solid bacillus is taken as viable while segmented bacilli as non-viable. Although there is a controversy over this, the ratio of non-viable to viable, **i.e.** a morphological index (M.I.), acts as a critical criterion of the inoculum. The model, however, has served a very useful purpose and can be used for study of chemotherapeutic agents. The drugs are added to the diet fed to the animals and a growth curve is plotted. A drug which is capable of stopping multiplication in the mouse foot pad can be said to possess chemotherapeutic or chemoprophylactic activity. In this model, it is also possible to distinguish a bactericidal drug from a bacteriostatic or bacteriopausal by feeding the drug either before inoculation; during the log phase of the organisms for a short period or over a prolonged period, to see whether bacteriostasis has been achieved.

Nine-banded armadillo is an animal model of great potential in the study of leprosy. The animals inoculated with **Mycobacterium leprae,** have developed infection almost as severe as in human lepromatous leprosy. The animals show a severe disseminated lepromatous leprosy, which histologically is comparable to lepromatous leprosy in man, except that the dissemination is more widespread. Acid fast bacilli could be shown to be present intraneurally just the same way as is found in humans. Since the model is very new, as yet there is no record of the use of this model for assessing the efficacy of chemotherapeutic agents in leprosy. In comparison with the mouse foot pad model, armadillo model should turn out to be better. In case of mouse foot pad, it takes almost 3 months before the infection begins to occur and the peak infection is seen at the end of six months. In the armadillo model, the lepra bacilli seem to multiply rapidly and disseminated disease is evident almost within a period of 10 to 40 months. It appears that for screening of compounds, this animal model may be useful in view of greater similarity with human disease.

Drugs used in treatment of leprosy as chemotherapeutic or chemoprophylactic agents : The age-old drug is D.D.S. Other additions are acedapsone or D.A.D.D.S., chlofazimine (Lamprene), long-acting sulphonamides, thiambutozine, rifampicin. D.D.S. continues to hold the sway as a drug of choice in the management of leprosy because of its low cost and infrequency of the emergence of sulphone-resistant cases. Its most inherent drawbacks are slow bacteriostasis, prolonged administration, inability to reduce the bacterial index very quickly, although the morphological index is brought down quickly. Ellard (1971) has reported that in spite of D.D.S. treatment, there are bacilli present in the smooth muscles and superficially located striated muscles, liver, bone marrow and into the nerves. This has got an important bearing, since their presence, may explain relapse. Thiambutozine, streptomycin, thiosemicarbazone are of doubtful use. Long-acting sulphonamides have certain advantages. They can be administered weekly. Some leprologists claim good results with these drugs particularly in tuberculoid forms of leprosy and consequent complicating neuritis.

As pointed out by Ellard, dapsone is a very good drug, because it is rapidly and completely absorbed, slowly eliminated and has a half-life anywhere between 15 h. and 53 h. (average 24 h.). After treatment with 1 mg/day to 300 mg. twice a week, viable bacilli fall to less than one per cent of the initial in 3 months period; MI falls to base line in about 4½ to 6 months. It has got a very good power of penetration in all tissues. However, dapsone does produce resistant strains. This was first noted by Rees and Petit in Malaysia ten years ago. As yet, there has been no trial with Rifampicin but with MIC of 0.3 ug/ml. in the treatment of patients, the drug has been found to be bactericidal, MI falling within 4 weeks in a dose level of 600 mg./day. Clofazimine 200 to 300 mg./day is almost equivalent to dapsone.

There is a definite advance in the treatment of leprosy from the demonstration of the activity of a dye-clofazimine (phenacine dye) against **Mycobacterium leprae.** The unique advantage of this compound is that the drug has got definite bacteriostatic activity in addition to having anti-inflammatory effect, as reported by Browne in 1965. It was shown by Shepard that there is a definite action in mouse foot pad. It was demonstrated to have anti-mycobacterial activity by Petit and Ridley. Azuley and colleagues (1974) have shown that Clofazimine is positively effective in sulphone-resistant cases. The drawback of this compound is, of course, its very high cost, and the fact that the drug accumulates into skin giving rise to coloration, particularly in light-skinned individuals.

Rifampicin is the newest entrant into therapy of leprosy. It is a very potent antibiotic having antitubercular activity. Rees and colleagues (1970) showed beyond doubt its efficacy in mouse foot pad infection. Rees subsequently reported in 1970 its activity and effectiveness in sulphone-resistant lepromatous cases. It produces invariably a very rapid reduction in the morphological index and is also fairly quick in reducing bacteriological index (B. I.). The rapid killing of **Mycobacterium leprae** is expected to reduce the incidence of complications, thought to be due to slow and continuous release of antigens of **Mycobacterium leprae** following a bacteriostatic action of D.D.S. Although the drug is said to be non-toxic, there are reports to suggest its hepato-toxicity and occurrence of thrombocytopenia. It is also very costly.

D.A.D.D.S. or acidapsone is comparable to D.D.S. Shepard **et al** (1968) reported a very short-term trial with this compound. Russel **et al** in 1971 and Sloan **et al** reported a longitudinal clinical trial with this compound in New Guinea and Micronesia. The drug is injected in a dose of 225 mg. every 70 days and gives rise to absorption of 2.4 mg. per day of D.D.S. given after an initial stage, a level above 50 nanograms per ml. M.I.C. for **Mycobacterium leprae** being about 20 nanograms per ml. This level of twice the M.I.C. level is maintained over a prolonged period. Five injections per year suffice to maintain a high antibacterial concentration of D.D.S. In the trial reported by Russel **et al**, they treated a total of 460 cases. Injections were well received with no local reactions. The incidence of leprea reaction was the same as expected with the standard dose of dapsone. The clinical response to therapy after 4 years in their trial was quite satisfactory in all patients. McRae and Roussel also followed up their patients of D. A. D.D.S. trial on the basis of M.I. and B.I. It was evident that the B.I. decreased very regularly and solid ratio also returned to base line within the first year. Concurrent administration of drugs such as thiambutosine and long-acting sulphonamides, thiosemicarbazone, clofazimine and rifampicin along with D.D.S. has also been tried in the treatment of leprosy, but failed to produce highly synergistic effect and particularly to prevent the possibility of development of sulphone resistance. The results were equivocal; probably there is no advantage in the combinations. However, in the Indian context, it is necessary to have a more extensive trial with drug combinations in view of the reported incidence of almost 20 per cent failures to D.D.S. therapy.

Problems of chemotherapy : Chemoprophylaxis of leprosy poses a number of problems. The disease is very slow in its onset and development; the drug has to be given over a prolonged period of time. The factors peculiar to chemotherapy of this disease are :

(1) Selection of patients

(2) Variable host-parasite relationship

(3) Properly matched control

(4) Criteria for monitoring the response

(5) Reduction in the period of infectivity

(6) Rapid tissue clearance of bacteria

(7) Development or otherwise of the resistant strains

(8) Problems of immune response

(9) M.I. as indicating viability of the bacteria

(10) Criteria of cure - clinical, immunological or bacteriological.

Any drug likely to be taken up as chemoprophylactic agent must be viewed in the light of the following considerations :

1. Minimum inhibitory concentration, M.I.C. **vis-a-vis** maximum tolerated dose of the drug (M.T.D.)
2. Characterisation of antileprosy activity, whether it is bactericidal, bacteriostatic or bacteriopausal, **i.e.** producing prolonged bacteriostasis
3. Toxicity in relation to M.I.C.
4. Metabolisation of the drug, particularly the problem of enzyme induction or the problem of accelerated metabolic transformation
5. Short-term trial
6. Long-term trial, to determine whether the drug can continue to produce prolonged action
7. To assess whether there is a response to M.I.

It must be mentioned that our present methodology is inadequate to finally assess whether in fact the assessment based on B.I. and M.I. reaching one per cent or base line respectively does render the patient non-infectious. Although infectivity in mice with an inoculum of $1x10^3$ to $1x10^4$ bacilli can no longer be demonstrated, there will still be less than 10^9 bacilli for, in order to demonstrate a definite viability, the total number of bacilli must be greater than 10^9. This must be accepted as a limitation till better methods are available. The pre-requisites of trial of a prospective chemoprophylactic, are as follows :

1. The population must be selected, which would have an expected incidence of new cases and this population must be large enough to yield valid data but still should be manageable for the trial
2. To identify all existing cases in the population, (in other words, surveillance,) and to detect them from those considered at the risk of developing the disease
3. To give chemoprophylactics to all non-cases
4. To observe subsequent incidence of new cases through frequent and complete examination of that population

(5) The problem of age at the start of contact : The success of a chemoprophylactic is determined by the age. It is much better in younger age group.

(6) Duration of contact : Shorter intermediate or longer duration of contact will determine the success rate of chemoprophylactics.

(7) The level of prophylaxis : The disease being slow, the prophylaxis has to be continued over a prolonged period; one has to think of assessment on the basis of adequate prophylaxis. In fact, this becomes a very big problem,

(8) To establish safety and economy and acceptability.

Considering all the problems, the planning of chemoprophylaxis trial becomes a very complex exercise.

The two important drugs, which have been used in the prophylaxis of leprosy, are : D.D.S. and D.A.D.D.S. D.D.S. or Dapsone was used as a prophylactic for the first time in Bombay in 1954 by Figueredo. Figueredo and Balakrishnan (1967) reported very good results with Dapsone. Out of a total number of 9,948 cases, 3,424 received D.D.S., while 6,524 contacts received placebo. Only 20 patients who received prophylactics, developed leprosy. Eighty patients developed leprosy in the control group, indicating a very high efficacy of D.D.S. as a chemoprophylactic agent. In this trial also, one more factor that became evident was that the younger age group showed better response as compared to the old age group. Dr. Figueredo reported that a reduction in the incidence of leprosy in the prophylactic group to be 48.1 per cent more than seen in the control group. Noordeen in 1969 reported a project on chemoprophylaxis started in 1966 at Chingleput. Seven hundred and eighteen contacts were studied for 5½ years. The contacts and the controls were very well-planned and it was a double blind trial. The contacts were equally divided between the control and the D.D.S. groups randomly after stratification by age and sex. They were almost well-matched. The difference in the incidence of leprosy between the two groups was highly significant. The chemoprophylactics had an effectiveness of 52.5 per cent. The maximum protection was seen in the age group of 5 and 6, while the rate of incidence in the control group was 74.3 per 100,000 person-weeks of treatment in the treated group; it was 35.5 per 100,000 person weeks of treatment in the prophylactic group showing almost a 50 per cent reduction in the incidence of leprosy. There are several points which emerged out of Noordeen's trial, though the chemoprophylaxis is ineffective in the early period of treatment, also ineffective in older children and contacts of untreated index cases and ineffectiveness in bacteriologically negative contacts.

As the duration of contact increases, the probability of getting leprosy in the control group becomes higher, while in the treated group, the probability of contacting the disease remains low. Upto 50 weeks of treatment, there is hardly any difference in the control and the treated groups.

D.A.D.D.S.

D.A.D.D.S. was tried as a prophylactic by Shepard **et al** (1968), Sloan **et al** in 1972, Russel **et al** in 1974 and Worth **et al** in 1973. According to Russel, a three-year trial in Mecronosia covered about 1509 people in three villages. They were given mass treatment with D.A.D.D.S. during the years 1967 and 1970. Annual re-examination of this entire population revealed that out of 9 cases appearing since the start of D.A.D.D.S. injection, only one was among 950 people who received injections of D.A.D.D.S. Even this case was subsequently proved to be sulphone-resistant. Eight cases in approximately 613 people, who received fewer than 12 injections, indicating that there was a significantly lower incidence of leprosy among those who received a full three years' course of D.A.D.D.S. It is pertinent to note that no case has appeared yet among the 300 or more children born since 1968 and who received D.A.D.D.S. therapy. The dose they used was 225 mg. every 75 days intramuscularly for all above the age of 6 ; between 6 months and 5 years, they used 150 mg. every 75 days, and they did not treat contacts between age of 0 and 5 months. They carried on the surveillance for detection of leprosy from 1968-73.

The most pertinent point in a trial of this type is to be able to break the process of transmission. If the prevalence falls below a critical level a risk factor in the transmission may become decidedly low. If this can be proved, the control of leprosy with D.A.D.D.S. administered to the contacts and for regular treatment of all patients is likely to pave the way for breaking the transmission. This will ultimately serve to control or eradicate the disease in an endemic population. The best approach, as pointed out by Wardekar, will be (i) immediate surveillance for case detection, (ii) prompt treatment of all cases (iii) chemoprophylaxis of the contacts with D.A.D.D.S. and treatment with combination of drugs like D.D.S., clofazimine or thiambutozine, in these bacilliferous cases with bacillary index of 2 plus 1 or more. Now these intensive measures can certainly cause eradication of the disease in a community. One must understand that when one undertakes trial of efficacy of prophylactics, an important factor that is likely to affect the rate of fall is the factor of case-detection. Dr. Wardekar's report on chemoprophylaxis of leprosy, which was made in 1963 with the standard dose of D.D.S. clearly proved a definite reduction in the incidence of leprosy in the control, **i.e.** the placebo group. This lowering was 41.9 per cent and this may certainly be due to better leprosy control programmes. However, that does not minimise the success achieved by Dr. Wardekar in the prophylactic group, where the reduction in the incidence was almost 90 per cent **i.e.** almost 48 per cent over and above what was seen in the control group. We have recently formulated a D.A.D.D.S. preparation and have undertaken a trial at Richardson Hospital, Miraj, and Acworth Leprosy Hospital. While the detailed trial will be reported elsewhere, we find that D.A.D.D.S. gives a fairly high concentration at the end of 35 days, but the concentration falls to almost 20 to 30 nanograms at the end of 65 days. We have, there-fore, given injections every 65 days. Ten patients in this group were studied ; the initial mean morphological index was 4.6 ranging from 1.3. to 9.01, while it was seen at the end of 30 days to be 0.8, ranging from 0 to 1.7.

More extensive drug trial is now in vogue, both at the Acworth Leprosy Hospital and the Mission Hospital, Miraj.

Chemoprophylaxis has to play a major role in the control of leprosy. Since, taking of D.D.S. tablets is associated with a high drop out rate in the patients as well as in the contacts, unless a very close supervision is maintained, D.A.D.D.S. injections, in contacts, may prove very helpful in breaking the cycle of transmission of disease. It is expected that one injection every 70 days may suffice to reduce the incidence of leprosy in the contacts of infectious cases.

The ultimate objective, **viz.** the eradication of leprosy, can only be accomplished by a multi-pronged attack, i.e. case-detection, education, and adequate treatment with D.D.S., clofazimine or, if possible, with rifampicin. Continuous treatment of patients over a prolonged period, at least not less than 5 years in case of tuberculoid and not less than 10 years in case of lepromatous leprosy, would be necessary. Education of the public and integration of leprosy in the total health programmes of the country and administration of effective, acceptable, cheap and logistically feasible drug to contacts are sine quanon for the control of leprosy. It is only then that it will be possible to eradicate the disease.

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Certain Problems in the Chemotherapy and Chemoprophylaxis in Leprosy

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Among several public health problems of this country, leprosy occupies a prominent place. Organised efforts have been made during the last 20 years to deal with this problem at the national level but it must be admitted that the position is still far from satisfactory. Recent estimates indicate that there may be anywhere between 3.5 to 3.7 million patients suffering from leprosy, in this country. Many factors can be held responsible for this poor showing. Students of leprosy who are conversant with the advances made in understanding this disease during the last 20 years, are aware of the large gaps in our knowledge that need to be filled. The object of the present discussion is to review the current position and indicate the areas along which further efforts require to be made. This paper will restrict itself to reviewing certain aspects of the chemotherapy and chemoprophylaxis of leprosy.

A review of the progress in the therapy of leprosy during the last century indicates that till the 1940's the position was at best unsatisfactory. A change for the better was brought about by the introduction of certain derivatives of the sulphone drugs in leprosy therapy, culminating with the use of the parent sulphone Diamino-Diphenyl-Sulphone (DDS) which is today the standard therapy for leprosy.

It is necessary in this connection to mention that the approach to the chemotherapy of leprosy has upto now been riddled with many difficulties. These are :

(1) The failure to cultivate **M. leprae** in **in vitro** systems, or otherwise obtain adequate quantities of the live organism free from contaminants, has made it difficult to obtain information on certain aspects like the chemical and biochemical architecture and specific requirements for its growth and maintenance. Such information if available, would have enabled a positive approach to chemotherapy, rather than the inferential or empirical approach being adopted today.

(2) The absence (till recently) of a suitable laboratory host capable of being easily and consistently infected with **Mycobacterium leprae,** made it difficult to test any drug claimed to be of use, other than in the human patients.

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(3) Such drug trials in human subjects were faced with certain restrictions rendering the interpretation of the drug effect difficult.

(a) Leprosy in the human subject presents a wide spectrum with varying degrees of immunological efficiency. Since it is difficult to clearly separate one from another, particularly in adjacent areas of the spectrum, it was difficult to decide whether any improvement with schedules of drug administration was due to the drug or the effect of immunity.

(b) Assessment of therapy was otherwise relatively limited and slow, as it depended on periodic clinical, bacteriological and histopathological evaluations. The bacteriological evaluation or the bacteriological index did not take into account differences between dead, dying and viable organisms, but was at best only a rough esimate of the total quantity of organisms at any one time. There was some improvement in the position with the introduction of the method of morphological index, but even so the rate of killing of **M. leprae**, which is the only certain index of drug efficacy, had to wait for suitable procedures to be elaborated.

Chemotherapeutic research in leprosy has been considerably facilitated by the availability during the last 15 years of a model of experimental leprosy infection in the mouse (Shepard, 1960). The use of this model enables one to ascertain whether any remedy claimed to be useful, is really effective without being required to be used in human beings. In the assessment of drug action this model enables monitoring of the rate of killing of **M. leprae**.

One of the remarkable findings with the use of this mouse model is that **M. leprae** from previously untreated cases of leprosy, is exquisitely sensitive to DDS (Shepard 1973). Plasma or blood concentrations in the mouse as low as 5 - 9 nanograms per ml. appear to be capable of inhibiting bacterial multiplication in the foot pad, and if these results are extrapolated into the clinical situation, would mean that sulphones in doses well below those commonly used in clinical practice should be adequate for treating bacterio-positive leprosy. Actual experience in therapy however is different and it would be necessary to investigate the reasons for these differences. Variations in the experimental procedure also enable one to ascertain whether a particular drug that is effective is bactericidal or bacteriostatic in action. This model has been applied very successfully in drug research in leprosy ever since it was first introduced in leprosy research.

An ideal drug for the treatment of leprosy should have the following properties : –

(a) The drug should be bactericidal and should be effective in a reasonable period of time.

(b) The drug should be free of any toxicity in the therapeutic dose ranges.

(c) It should be able to clear the body of the large load of fragmented and dead organisms.

(d) It should be such against which no resistance is capable of being developed.

(e) The drug should be cheap, easily administrable and available in suitable stable preparations.

None of the drugs that are available currently for the treatment of leprosy fulfil all these requirements and the most effective ones at best fulfil only a few of these.

Sulphone drugs and in particular orally administered Diamino-diphenyl-sulphone, have now been in use for sufficiently long in the therapy of leprosy. Numerous well planned clinical trials with various dose ranges and various schedules of administrations have been conducted. These studies indicate that such orally administered sulphones are therapeutically effective in a wide range of doses and with different schedules of administration. These qualities coupled with the fact that sulphones are cheap, easily available and relatively non-toxic even with prolonged administration, have made this drug the standard remedy for the treatment of leprosy. Despite these advantages however, it must be mentioned that there are certain shortcomings with sulphone. The drug is essentially a bacteriostatic remedy and acts very slowly requiring several years of administration before adequate clinical and bacteriological improvement is brought about. Even after such prolonged administration one is not sure that the body is free of mycobacterium leprae, because it has recently been shown that viable organisms which are susceptible to the action of sulphones, are still recoverable from certain sequestered sites from the body after many years of sulphone administration under sanatorium conditions. A certain percentage of cases of leprosy undergoes relapse even while under sulphone therapy, and not all these are due to the development of drug resistance. Needless to say drug resistance (Pettit **et al** 1966), **i.e.** the inability of mycobacterium leprae to be inhibited by adequate concentrations of sulphones, has been discovered and is capable of assuming serious proportions. One other disadvantage with sulphones is the likely precipitation of episodes of activity which are spoken of as "reactions" and which require separate therapeutic attention.

Before discussing some of the above shortcomings it may be worthwhile to briefly review the alternate drugs that have been used so far in the treatment of leprosy. Anti-tuberculosis drugs including both Streptomycin as well as Isonicotinic Hydrazide have very limited application and are useful in certain special situations in leprosy. Long-acting sulphonamides have been tried out in certain situations but these drugs are expensive and do not pose any advantage over orally administered DDS. There are two other remedies that require mention and these are certain derivatives of Diphenyl-thiourea, and Thiosemicarbasone. Both these drugs were considered as suitable second line drugs for the treatment of leprosy but for long term use they are unsuitable as there are disadvantages with both these drugs including the development of drug resistance in short periods.

It is therefore obvious that the therapeutic armamentarium against leprosy is very limited and that there is an urgent need to develop more drugs that would be useful in this disease. Two recent introductions in the therapy of leprosy will now be dealt with. These are : Clofazimine (also known as Iamprene—B.663) and Rifampicin. The former is a synthetic drug and over the course of the last 10—15 years has been established as a useful remedy both in the therapy of leprosy as well as in dealing with lepra reaction. The drug is used in doses of 100 to 600 mg. per day in oral administration and side effects include pigmentation, dryness and itching of skin, and occasional gastro-intestinal disturbances. These side effects are more than compensated by the therapeutic action of this drug. The mode of action of this drug is yet not very clear but it appears to be by interfering with intra-cellular protein synthesis in the mycobacterium. The drug is very useful in certain situations in leprosy, but unfortunately is in short supply and is expensive. The other drug Rifampicin is a synthetic antibiotic and is credited to be the first known bactericidal agent against **M. leprae**. The mode of action of this drug also appears to be by interference with certain aspects of intra-cellular protein synthesis and in therapeutic trials carried out so far it has been shown to be rapidly active especially in its ability to kill M. leprae rapidly. Toxic effects like those on the liver and bone marrow have been reported but the drug has as yet not been used extensively in leprosy because of its prohibitive cost and of its being available in very limited quantities.

Several aspects of sulphone therapy such as the effective dose, duration of treatment, the question of maintenance therapy etc., will not be discussed here because of limitation of time but there are two topics that merit consideration. These are : the occurrence of reactions during therapy and the development of sulphone resistance.

Reactions : The occurrence of episodes of inflammatory activity during the course of sulphone therapy for leprosy is serious enough to warrant special mention. These reactive episodes vary from very mild to severe life-threatening forms and are stated to be brought about by deposition of immune complexes in the walls of blood vessels in certain sites in the body. The therapy of these reactions poses difficulties as it has to be carried out with as little interruption as possible of the specific therapy for the disease. Two recent introductions in the therapy of reactions are : (a) Clofazimine, and (b) Thalidomide (N-phthalimido-glutarimide). Both these drugs are useful in controlling reactions and inducing sulphone-sensitive patients to take optimum doses of DDS for treatment.

Drug resistance : It has been shown that certain populations of **M. leprae** are unaffected by concentrations of sulphone that are capable of being achieved with maximal clinical dosage. This subject will be dealt with in detail later in this symposium, and it is only necessary here to deal with this problem in so far as its relation to therapy is concerned. The mono-therapy for leprosy that has been in vogue after the introduction of sulphones is considered to be one of the important factors in the development of such resistance. Other reasons include insufficient dosage and irregular or interrupted treatment. Whatever may be the mode of occurrence of such drug resistance it creates serious problems both in the therapy as well as in control of leprosy. With our restricted therapeutic armamentarium at present such cases can be treated either with Clofazimine or with Rifampicin. The development of such drug resistance is a major problem in leprosy calling for search for newer and better drugs.

Specific areas of future research in chemotherapy : The scientific developments in leprosy research during the last 15 years have been very helpful in dealing with the problem of chemotherapy in leprosy. However there are still certain limitations to the technical advances mentioned above. The experimental mouse model is an instance of such advance which has certain limitations. These limitations are occasioned by the short life span of the mouse, the natural immunity mechanisms in the animal, and the fact that the mouse is sensitive to leprosy infection only within certain limits. Other animal models are therefore required to be developed. The armadillo infection (Kirchheimer **et al,** 1972) which is a more recent development may help to get over some of the difficulties faced in the mouse. One of the important requirements for a suitable experimental animal is the ability for it to be infected with very few viable **M. leprae.**

It has been indicated earlier that the lack of information on certain intrinsic characteristics on **M. leprae** has been responsible for difficulties in a positive approach to chemotherapy. This difficulty could be got over if it is possible to cultivate this organism in **in-vitro** systems. The armamentarium of leprosy chemotherapy is extremely limited and the development of newer drugs therefore assumes high priority. In such drug development it would be very useful if drugs could be found that could act rapidly and effectively. The recognition that the treatment of a bacterial disease with a single drug can facilitate the development of drug resistance calls for a change in the therapeutic schedules and the use of two or more drugs at the same time. In like manner the current schedule of a long drawn out induction of therapy requires to be shortened, so as to achieve maximum doses very rapidly. Other fruitful areas of investigation in chemotherapy include the mechanism and prevention of reactions and the identification of reasons for relapses in leprosy.

Chemoprophylaxis : The concept of prevention of a bacterial disease by prior administration of drug is not new to leprosy and the possibilities of such chemical control materialised when DDS became available for the treatment of this disease. In a sense the mass therapy with sulphones which aims at reduction of the total quantum of infection is a measure for protecting the healthy population from the disease. The observation that the administration of sulphones to persons running the risk of getting leprosy can either prevent or delay the occurrence of the disease, was the starting point for chemoprophylaxis, and a well planned, properly organised, double-blind prophylactic trial that was carried out by the Central Leprosy Teaching and Research Institute revealed that child contacts with a high risk of getting leprosy were protected to the extent of about 53 per cent by such chemoprophylaxis (Noordeen, 1968). These initial observations posed further questions such as the duration of such chemoprophylactic sulphone administration, the optimum dose or doses, the extent to which such protection continues after cessation of drug administration and the extent of such protection to contacts who are not high risk subjects. These questions are being studied in another trial at the Institute which is expected to conclude shortly. It may be mentioned here that the results obtained from these chemoprophylactic trials are not capable of any automatic translation to public health practice, since there are many other questions that will require to be answered before considering large scale chemoprophylaxis.

Recently we have available a depot preparation of sulphone in the form of Acedapsone. This preparation which requires to be administered intramuscularly has been shown to be capable of maintaining blood levels of sulphone adequate for bacteriostasis, when such injections are administered once in about 75 days. Therefore there are considerable logistic advantages over orally administered sulphone with the use of this preparation and a suitable trial is under progress. It is however necessary to bear in mind that blood levels reached with Acedapsone are low compared to oral sulphones, and that it is necessary to be watchful for the emergence of drug resistant **M. leprae**. If it is possible for a suitable safe and workable measure of chemoprophylaxis to be evolved and to be used as a public health measure, considerable benefits will accrue to the endemic population in this country.

It hardly requires emphasis that chemotherapy and chemoprophylaxis in leprosy are the two most important weapons that we possess today in dealing with the disease and this is particularly so in the absence of any specific vaccination procedure. This has been recognised by agencies concerned with dealing with the disease, and it is hoped that concerted efforts in these two aspects which are being made by international agencies like the W.H.O., and which reflect the concern of these bodies towards the serious state of the problem, will bear fruit some time in the near future.

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Drug Resistance in Leprosy

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Introduction

Until 1949 there was no effective drug to treat leprosy. The discovery of D.D.S. (Dapsone) as an active antileprosy drug in the dosage of 100 mg. per day is a great landmark in the history of the disease (Lowe 1952). Even so chemotherapy of leprosy lagged behind the chemotherapy of tuberculosis and other bacterial diseases because until the year 1960 **M. leprae** the causative organism could not be cultured. Any drug that had to be tested had to be tried only in leprosy patients and that too on the basis of their action against **M. tuberculosis**. This method had its drawbacks, for all anti-tuberculous drugs were not effective against **M. leprae**.

Further there are some unusual features of leprosy which are to be taken note of in any drug trials.

(1) Since the progress of the disease is slow and gradual the clinical response to a drug also seems to be slow. It takes an year or more of treatment before any obvious clinical response can be detected.

(2) It is known that **M. leprae** that are killed by the drug remain in tissues for a long time. The organisms have a half life of about 100 days in lepromatous leprosy (Ridley 1967 ; Shepard **et al** 1968). Therefore, the immediate effect of the drug cannot be estimated by just assessing the bacillary population. Recently it has been found that effective antileprosy drugs produce granulation and fragmentation of bacilli and these granular bacilli cannot be cultured in the footpads of mice (Shepard and McRae 1965). Therefore it is possible now to assess fairly quickly the efficacy of a drug by determining the Morphological index (M.I.) which is the percentage of solid or uniformly stained bacilli.

(3) The disease manifests itself in a wide variety of clinical forms depending on the patient's immunological status. It can be a mild form like tuberculoid leprosy having no demonstrable bacilli or it can be a very malignant form like lepromatous leprosy with many bacilli present throughout the skin and mucous membrane.

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Therefore, drug studies should be conducted on lepromatous patients who have a uniform immunological response and contain a large number of bacilli that can be periodically tested (Waters and Rees 1962).

Treatment of Leprosy

Diamino Diphenyl Sulphone (D.D.S.) : D.D.S. is the sheet anchor in the treatment of leprosy and is the drug of choice in all types of leprosy patients. There are many advantages in using the drug :

(1) It is given orally in tablet form in a dosage of 50 to 100 mg. once daily and therefore is easily administered.

(2) The complications directly related to the drug even after long periods of treatment are very few and therefore medical supervision required is minimal.

(3) The cost of the drug is only Rs. 5.00 to Rs. 10.00 per year per patient and is therefore very cheap.

(4) It is now known that within 6 months of treatment no cultivable bacilli can be isolated from most of the lepromatous patients.

(5) Most, if not all, patients getting regular antileprosy treatment will ultimately become negative for bacilli. However due to certain unusual features of the disease it may take more than 5 years to achieve complete negativity (Lowe 1954 ; Roy 1956).

Recently in an analysis of all 22 lepromatous patients in our institution who have had antileprosy treatment regularly with us for 15 years, we found 19 are negative for bacilli most of them for several years, and the other 3 were still positive because for some reason or other their treatment was interrupted.

D.D.S. Resistant M. leprae : Clinical evidence of D.D.S. resistant leprosy was available even as early as 1953 (Wolcott and Ross, 1953 ; and personal observation 1959). The presence of resistant strains was proved beyond doubt using experimental methods only in 1964 (Pettit and Rees 1964). Since then several reports of D.D.S. resistant strain of **M. leprae** from different countries have appeared (Adams and Waters 1966 ; Rees 1967 ; Jacobson 1973 ; Taylor **et al** 1974).

Resistance to D.D.S. was initially suspected following repeated clinical and bacteriological examinations when no improvement was noticed despite a fairly long period of treatment. Then it was confirmed using mouse foot pad culture techniques.

The 3 group of animals used for the experiment were given an injection of 10^4 **M. leprae** isolated from the patient suspected of D.D.S. resistance and each group of animals were given food pellets containing 0.01 per cent, 0.001 per cent, 0.0001 per cent of D.D.S. respectively. The control animals injected with the organisms were given normal diet. At the end of 6, 8, and 10 months, 2 animals from each group were sacrificed and bacilli were harvested. If the organisms grew in all animals both experimented and control, they belong to a highly resistant strain. If the organisms grew only in control animals they are of a strain highly sensitive to D.D.S. If they grew in control animals and in those receiving low concentrations D.D.S. in the diet the organisms are only mildly sensitive to D.D.S.

In our experience with 39 patients, 6 experiments failed in that no growth was obtained in all 4 groups of mice. Fourteen were found to be highly sensitive to D.D.S. Seven were mildly sensitive to D.D.S. and 12 were resistant.

Waters **et al** (1975) have detected 98 patients from Malaysia resistant to D.D.S. using experimental methods. Clinical evidence of resistance was seen from 5 to 24 years after D.D.S. treatment. More than 2/3 of patients remained negative for many years before relapsing with D.D.S. resistant strains of bacilli. Low dosage and intermittent administration of D.D.S. favoured sulphone resistance.

In our experience 6 of the 12 from whom resistant strains were isolated had episodes of reaction and were given intermittent D.D.S. Some had low dosage of D.D.S. for varying periods. The resistant strains were isolated 4 to 30 years after commencement of treatment. It is interesting to note that there was also an instance of a patient who had D.D.S. 100 mg. regularly and remained negative for 12 years and then relapsed with organisms resistant to D.D.S.

D.D.S. resistance has also been reported from other parts of our country (Roy Chaudhury and Desikan 1975). There is no doubt that there are significant number of patients in different parts of our country who are D.D.S. resistant but are not detected for lack of adequate facilities. However, it must be pointed out that although D.D.S. has been in use for over 25 years the resistant strains of **M. leprae** now known in our country are a small number. The main reason may be that the dosage of D.D.S. given is 50 to 100 mg. per day which is 50 to 100 times the effective dosage against **M. leprae.**

Although primary resistance to D.D.S. is not yet reported, the possibility of emergence of it soon cannot be disputed.

Alternate Drugs

Although Thiambutosine (Diphenyl Thiourea, DPT, Ciba 1906) and Thioacetasone (Thiosemicarbosone, TB1) are available as alternate drugs, resistance to them have been reported much sooner than in D.D.S (Davey 1955, 1960 ; Lowe 1954).

Thiambutosine has been used as an alternate drug especially in patients allergic to D.D.S. It has been found that in D.D.S. resistant patients resistance to DPT developed within 16 months to 4 years after commencement of therapy. This is a marked contrast of 5 to 24 years (an average of 16.8 years) for the development of D.D.S. resistance (Waters **et al** 1975). There is also cross resistance between Thiambutosine and Thiosemicarbosone.

The chief secondary drug for use in leprosy is Clofazimine (B. 663, Lamprene). Patient receiving this drug develops a reddish brown pigmentation (Browne 1965). The drug is administered in daily doses of 100 mg. daily and is also effective in controlling reaction of Erythema Nodosum Leprosum. In mice it is active against **M. leprae** at 0.01 per cent concentration in diet. Although this drug is in use for nearly 10 years no resistant strains have yet been reported.

Rifampin has been tried and excellent bactericidal effect has been recorded. After 600 mg. of rifampin daily for 7 to 14 days the bacilli obtained from the patients were no more cultured in mice (Shepard **et al** 1972). However the cost of the drug is very high. Result of long term trials are awaited.

Conclusion

It is important to treat patients with combinations of drugs to reduce incidence of drug resistance. Combined therapy in mice have been reported (Shepard 1972). Dapsone, Clofazimine, Ethionamide when tested individually had bacteriocidal activity and in combination potentiated each other's action. But no human experiments on combined therapy are reported.

It is also important and necessary to find new drugs that are cheap and easily administered to supplement D.D.S. It may not be very long before primary resistance to D.D.S. may emerge and there may be increasing number of patients who may not respond to D.D.S.

Further a method of treatment which will eliminate killed bacilli quickly from the body without producing harmful results should also be evolved.

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Immunoprophylaxis in Leprosy

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Gravity of the situation arising from the endemicity of leprosy and its high prevalence in many parts of the country is well recognized and necessity of prophylactic measures for the control of the disease is being seriously considered. Chemoprophylaxis with sulphones has been shown to be effective but its role in mass application as a part of leprosy control is rather limited. Attempts at the immunoprophylaxis of leprosy made in experimental animals and in human subjects will be summarised in the followings.

Experimental Immunity : Experimental immunity in leprosy has been studied in mice. It has been shown (Shepard, 1960) that when a small number of viable **M. leprae** are inoculated into hind footpad of immunologically competent mice the organisms undergo multiplication, achieving a ceiling of about $10^6 - 10^{6.3}$ organism per footpad in about 100 to 150 days. The experimental infection can be compared with the **M. leprae** infection in humans in having a long incubation period. Even though the experimental infection cannot be compared with human leprosy it serves as a useful model for chemotherapeutic and immunological studies. The reduction in the number of **M. leprae** growing in the footpad of immunized animals as compared to controls has been taken as the criteria of protection (Shepard 1965 and 1966). Using this model, heat killed vaccines prepared from various mycobacterial cultures had been compared for the protective action and **M. tuberculosis** was found to confer greatest protection (Shepard, 1968). Living BCG was found to be equally affective and the effect did not significantly alter when the organism were heat killed (Shepard 1968). Protective action of BCG vaccination has been investigated in detail (Shepard, 1965 1966 ; WHO Memoranda, 1973). Vaccines given 1 or 2 months before the challenge afforded significant protection against **M. leprae** but vaccine given immediately after the challenge did not provide protection. It was, however, more interesting to note that the vaccine given after the challenge, during the logarithmic phase of growth of **M. leprae** caused protection upto the same level as provided by the vaccine given before the challenge. In view of these observations the authors had expected that BCG vaccination given early or later in the inculation period of leprosy in humans would provide protection. While comparing the potency of different BCG vaccines Shepard (1968) demonstrated that the freeze dried preparations were as effective as the vaccine prepared from freshly harvested organism. Studies on the route of administration with living BCG vaccines have shown the intravenous route to be most effective although the results did not significantly alter when intra-dermal or intra-peritoneal routes were employed (Kawaguchi, 1972). As already mentioned earlier and as also illustrated by representative data of Shepard's studies (Shepard, 1968 ; Table I) protection in the experimental mice model means only significant and not a substantial reduction in the multiplication of the organism or complete inhibition of its growth.

Table I. Amount of protection offered by BCG vaccine (Glaxo).

Vaccine Dilution	Lo$_{810}$ (AFB/Mouse)		
	Vaccine	Saline	Protection
1 : 1	5.55	6.18	0.76
1 : 10	5.68	6.24	0.63
1 : 100	6.08	6.38	0.23

Source : Shepard C.C. 1965. **Bull WHO 38,** 135.

Reinfection studies : In a different series of experiments protection was studied in mice preinfected in one of the hind footpads against challenge in the opposite footpad. Some of the early studies on reinfection (Levy, 1975) failed to show any protection in mice infected with **M. leprae** against homologous challenge. Subsequent studies of Kawaguchi (1972), and other investigators (Levy, 1975) have shown against varied degree of protection in mice preinfected with **M. leprae.** BCG and **M. murinum M. leprae** challenge. A recent report of levy on reinfection experiments not only confirms the protection extended by primary infection but also provide explanation for the conflicting results obtained by earlier investigators. Mice were inoculated with a standard inoculum of about 5000 **M. leprae** and challenged with a similar dose of inoculum at intervals after the primary infection. In control mice the primary infection reached a plateau level of about 10^6 AFB per footpad in about 90 to 112 days after which the multiplication is arrested due to operation of cellular immunity and the number starts declining. When the secondary inoculum was given at this stage or afterwards the organism showed a much reduced multiplication rate in comparison to that observed in the uninfected controls and the total number of organism remained very low. In mice given secondary infection between 17 to 47 days before attainment of peak level, although the multiplication was slower than in controls, the number of organism reached near about the same level as observed in uninfected controls. In mice inoculated with the secondary infection within a few weeks after the primary infection the rate of multiplication of the organism in secondry inoculation was similar to that of the primary infection and there was not protection at all. In another experiment it was demonstrated that the time required for reaching the plateau level was related to the dose of inoculum, that is, lower was the inoculum higher was the time taken. It was evident from these experiments that the dose of primary inoculum and the multiplication phase of the primary infection at the time of the secondary challenge are decisive factors in the determination of protection against the challenge. The study of Levy and others have also indicated that the plateu level of 10^6 organism has to be reached for expression of immunity (Levy, 1975). Multiplication apparently increases the antigen concentration but it is not yet clear whether this concentration of antigen is required to stimulate proliferation and sensitization of the lymphocytes or to attract sensitized lymphocytes and activated macrophages (Levy, 1975).

Studies made at the C.D.R.I., Lucknow, (Gupta and Mathur, 1964), in experimental leprosy in rats have shown superiority of an atypical mycobacteria, **M. kansasii** over BCG in providing protection against **M. leprae murium**. Protection was 62.5 per cent in **M. kansasii** vaccinated rats whereas the figure was only 45 per cent in the BCG group. With regards to size of leprae, histopathology of lesions, leprosy index and leprae index also the picture was better in **M. kansasii** vaccinated animals. Preinfection of mice with unrelated organism (Krehembull **et al** 1964) like **Toxoplasma gondii** and **Bensonvitia jellisonii** has also been shown to provide protection against **M. leprae** challenge. Protection is however, of lower degree than provided by mycobacterial species. The protection with **T. gondii** is enhanced when the Toxoplasma antigen is given locally in the foot-pad. It may be recalled that mice infected with **T. gondii** have been shown to be resistant also to **Listeria** and the resistance is operated through activated macrophages which kill the **Listeria** organism.

Mycobacterium marinum infection in mice had been suggested as a useful model (Ng **et al**, 1973 ; Shepard and Habas, 1967) for studying the immunity against **M. leprae** mainly because of its low temperature growth optimum (32-34°C) but its very rapid multiplication rate, inflammatory response and tendency to spread systemically appear to contra-indicate its use for such studies as suggested by Collin **et al** (1975).

Human Trials : Efforts at immunoprophylaxis of leprosy in humans have been handicapped primarily because of limitations in procurement of **M. leprae** antigen in large amounts. Multiplication of these organisms has so far been carried out in mouse foot-pad (Shepard, 1971) only ; recently 9 branded Armadillo, an animal inhibitating South America has been claimed to be better system for cultivation of **M. leprae in vitro** (Storrs 1971 and 1974) culture of the organism in synthetic media have not so far been successful. A recent report (Jadin, 1955) suggests the possibility of its cultivation in a free living amoeba **Acanthamoeba culbertsoni.**

Attempts at immunoprophylaxis against leprosy have therefore, beenrestricted to trials with BCG. Three major trials on BCG vaccination has so far been conducted in Uganda, New Guina and Burma respectively.

The Uganda trials (Brown **et al** 1968) were conducted by the United Kingdom Medical Research Council between September 1960 and September 1970 on child contacts and relatives of known leprosy cases. About 8000 subjects were included in vaccinated and control groups each. By the end of the fourth follow up in 1970, 201 cases of leprosy were detected in the unvaccinated children of the primary intake. In vaccinated group the figure was 40. This shows 80 per cent reduction in incidence of leprosy in BCG vaccinated subjects. The results of the first three follow up examination are given in Table II. The efficacy of BCG was not shown to be restricted to any sex or age groups. Although these results appear to be quite encouraging a generalized conclusion can not be drawn yet, primarily, because of a decreasing trend of incidence of leprosy in South Africa, most probably, as a result of chemotherapy, as indicated by the conductors of the Uganda trials.

Table II. Summary of results of BCG field trials in Uganda*.

	Follow up examinations			
No. of children in trial	First upto Mar. 1964	Second Mar. 1966	Third Mar. 1968	Total
Control	8071	9036	9036	9036
BCG	8691	9052	9052	9052
No. of Leprosy cases for thousand control	89(11.6)	54(6.6)	31(3.41)	144(19.3)
BCG	18(2.2)	1 (0.1)	8 (0.9)	27(3.0)
Reduction in Incidence attributable to BCG vaccination (%)	80	98	74	84

*Brown **et al** 1968. **Br Med J, 1, 24.**

In the New Guinea trials (Scott **et al** 1966) carried out in Karimai between 1963 and 1969 on about 5000 persons, the protection by BCG was observed in 46 per cent for the total population. Protection was equal in all the sexes but incidence of protection was slightly higher **i.e.** 56 per cent in the age group between 5 and 29 years.

The Burma trials (Bachelli **et al** 1973, 1974) were started by WHO in August 1966 in child population exposed to leprosy in household or elsewhere in highly endemic area. Till the end of March 1973 at a total of 28,220 children below the age of 14 years were included in the trials and subjected to varying periods of follow up with a minimum of 5 and maximum of 8 years. The number of persons, years of deservation for the BCG vaccinated and control groups were 83,283 and 82,978 respectively. Till the 8th follow up examination, completed in March 1973, 425 cases of leprosy were detected in the Control Groups against 343 cases in the BCG Groups, giving incidence rate per 1000 persons-years of observation of 5.1 and 4.1 respectively for the two groups. BCG, thus gives 20 per cent protection in the vaccinated groups. The protective effect of BCG at various follow up examination has been summarized in Table III. The maximum protection by BCG was observed in the fifth follow up. It may also be mentioned that valid comparison of the results can be made only upto fifth follow up, since only a part of the study population was subjected to further follow up examination. A slightly higher incidence of leprosy in BCG groups than the control in first follow up examination has not been regarded statistically significant, and has been attributed to a chance occurrence or to boosting effect of the vaccine by the conductors of the trial. An analysis of the data in relation to age groups would indicate maximum protective effect of BCG in children in the age group of 0-4 years where 44 per cent protection was observed during the fifth follow up (Table IV). The value however, decreased to 38 per cent by the ninth follow up examination. Incidence of leprosy among children of higher age groups, was similar in vaccinated and non-vaccinated groups and no significant protection by BCG was observed in the household contacts of leprosy patients. BCG vaccination also did not affect the evolution of leprosy in detected cases as the distribution of the forms of leprosy was similar in the two groups. In none of the groups a single case of lepromatus leprosy was diagnosed during the trial period, probably, because all the detected cases received treatment. During the fifth follow up it had appeared that protection by BCG was to a greater extent in males than in female children. A further analysis of sex differences in the various age groups did not reveal any consistent pattern, which could be regarded as indicative of confinement of efficacy of BCG to any particular sex.

The status of tuberculins reaction at the intake did not appear to have any influence on subsequent development of leprosy in vaccinated and control groups. The lepromin reactions in relation to the age at intake was consistently stronger in vaccinated children although the difference considerably reduced in higher age groups. Lepromin reaction in relation to age of onset did not significantly differed in the BCG and control groups.

The results of the Burma trial thus show a limited protection by BCG in lower age group children who are either not been exposed to the **M. leprae** infection or are

Table III. Number of Leprosy cases and protection in each follow up in Burma Trial*.

Follow up	No. of Leprosy cases		Protection
No.	BCG group	Control group	%
1	82	71	—15
2	70	89	21
3	61	86	24
4	55	68	19
5	31	63	42
6	26	25	— 4
7	11	24	54
8	7	15	53

*Bachelli et al 1974. **Bull WHO, 51,** 93.

Table IV. Protection by BCG in different age groups at the end of 5th and 8th follow up in Burma Trial* .

Age at intake		Control group			Vaccinated groups			
			Incidence	Rate %		Incidence	Rate %	
0—4	5th follow up	20695	66	3.2	21133	38	1.8	44
	8th follow up	32725	82	2.72	33201	56	1.7	38
5—9	5th follow up	20113	141	7.0	20100	137	6.8	3
	8th follow up	29873	192	6.43	29902	163	5.45	15
10—14	5th follow up	13212	118	8.9	13172	110	8.4	5
	8th follow up	20381	144	7.07	20181	124	6.14	13

*Bachelli et al 1974. **Bull WHO, 51,** 93.

in the early stages of the incubation period of the infection. The results are not significant and the investigators of the trial do not consider it likely that BCG could substantially affect the pattern or trend of leprosy in the trial or a similar are and do not recommend the nation wise use of BCG even in children of even the lower age group in which some protection was observed.

Approach suggested : Results of the experimental immunity in mice have shown the efficacy of homologous antigens (Kawaguchi, 1972 ; Levy, 1975) against **M. leprae.** Still more encouraging are the results on the effectivity of dead vaccines against leprosy (W.H.O. Memoranda, 1973) as well as malaria (D' Antonio, 1972) in experimental animals, particularly because use of alive **M. leprae** vaccine will not be a practical proposition in humans. Investigation may be taken up with dead **M. leprae** as such or after fractionation. Superiority of fractionated antigens in comparison to the whole homogenate has been demonstrated with regards to protective immunity in guineapig's against **Entemoeba histolytica** (Krupp, 1974). Nucleic acid extract of **M. tuberculosis** has been recently shown to confer immunity against **M. tuberculosis** (Youmans and Youmans, 1966 ; Rochelle **et al** 1973) in mice. Moreover, we know that all the antigens present in an organism do not participate in protective immunity. On the contrary some of the antigens may interfere with the action of protective antigens. Fractionation may increase the activity of protective antigens by eliminating such undesirable antigens. Until a suitable method for large scale cultivation of **M. leprae** is evolved these investigations may be restricted to animal experiments. Since BCG has shown a certain amount of protection, studies on fractionated antigens may also be extended to BCG or even **M. tuberculosis** $H_{37}R_A$.

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Problems and Perspectives in Research on Leprosy*

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A number of problems are posed in leprosy. Pertinent to the subject of this Symposium, the following can be enunciated.

I. Search for new drugs : One of the most urgent needs is to have alternate, effective and cheap drugs for treatment of leprosy. Sulfones have served well in the past two decades but mutants resistant to this drug have appeared and an increasing number of cases are seen in control programmes which fail to respond to this drug. The diagnosis of a DDS-resistant case is currently based almost entirely on clinical experience and it is not unusual that many months elapse before a case is classified as possibly a sulfone-resistant type. Meanwhile the patient infects several others with a strain of bacteria not curable by the usually employed drug. It can thus be expected that the number of cases resistant to DDS will grow in number in years to come.

Amongst the alternate drugs currently available, Rifampicin is one of the most effective. It is however, fairly expensive and is beyond the reach of most Agencies for routine use.

Consequently two problems are posed :

(i) The need to have quick ways of screening patients harbouring DDS-resistant strain of bacteria ; and

(ii) The need to have other drugs which are cheap, producible in large amounts and be atleast as effective as DADS if not more.

Being given that sulfones would most probably be acting as competitive antagonists to para amino benzoic acid, this metabolite should be required by **M. leprae** either for synthesis of folic acid or other entities. Compounds with better partition coefficient through lipidic environment and counteracting PABA in an alternate manner may serve as more effective compounds in the sulfone series. These compounds would however remain essentially bacteriostatic and perhaps it may be more profitable to devise an attack on alternate sites to achieve bactericidal effects. Information on metabolic characteristics of this bacteria is scanty, mostly because it has not been possible to cultivate **M. leprae** in a synthetic medium. It may be worthwhile to enquire whether the knowledge gained on **M. tuberculosis** (and its avirulent and attenuated strains) is applicable at least in part to this organism.

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*Gist of the comments made in the Symposium.

Some studies (Prabhakaran and Kirchheimer 1966) have shown that **M. leprae** is distinguishable from other mycobacteria in possessing an enzyme DOPA oxidase. The functions of this enzyme in this bacteria are not known. Compounds directed against this molecule could be tried in experimental systems for a possible selective anti **M. leprae** action.

It is not unlikely that drug companies and National Research Laboratories have a stock of potential anti **M. leprae** drugs awaiting screening. The mouse foot pad has served as a very useful method for this purpose ever since Shepard (1960) and Rees **et al** (1964) described this system. It requires, however, organized facilities for such testing. Moreover, several months are necessary to obtain the answer. There is need to evolve simple methods for first line screening of drugs. For this purpose it may be appropriate to investigate the feasibility of using the system described by us about two years back (Krishnan and Talwar, 1974 ; Talwar **et al** 1974). The system consists of using human macrophages as host cells for growth of **M. leprae.** These cells are derived from peripheral blood monocytes. Twenty ml. of blood can furnish about 15 - 18 Leighton tubes. The cultivated macrophages phagocytose **M. leprae** actively and are endowed with active metabolic machinery. The metabolic growth of the bacteria can be monitored by selective incorporation of ^{3}H-thymidine. Normally the macrophages being the end cells, are devoid of thymidine kinase and are unable to incorporate this radioactive precursor into DNA. The bacterial cells however, require to synthesize DNA as a prerequisite to division. The use of this radioactive precursor in the experimental protocol described previously enables a sensitive measurement of the metabolic growth of **M. leprae** within a natural host cell as a function of the environment. Drugs which do not require **in vivo** metabolism for getting converted into active compounds could perhaps be used in the medium for assessing their effect on the growth of the bacteria. The cultivated macrophages can be maintained **in vitro** along with phagocytosed bacteria for several weeks. Additional information can also be obtained on the degranulation and digestion of the phagocytosed bacteria by appropriate stains and histological examination.

II. Nerve Damage :- Many disabilities in subjects afflicted with leprosy arise from a loss of sensation. Nerve damage is more acute in tuberculoid than in lepromatous leprosy subjects. It is further seen that nerve damage is invariably precipitated in subjects with reactions. These observations suggest the possible involvement of immunological mechanisms in development of nerve lesions. The mechanisms are however far from clear and further research is required to elucidate these. The knowledge gained from such studies should have repercussions on our management practices and on our therapeutic approaches in this disease.

III. **Immunotherapy :** A number of studies during the past decade have indicated a deficit of cell-mediated immunity in lepromatous leprosy subjects (Turk and Bryceson, 1971 ; Bullock and Fasal, 1971 ; Godal **et al** 1971 and 1972 ; Talwar **et al** 1972 ; Mehra **et al** 1972). The depression is of two types, one of which is secondary to infection and is reversible by diminution of the bacterial load (Mehra **et al** 1972; Nath **et al** 1974; Godal, 1974). Attempts have been made to restore this deficit by (a) allogeneic lymphocyte infusion (Lim **et al** 1972; Saha **et al** 1975), (b) transfer factor (Saha **et al** 1975; Bullock **et al** 1972) and thymus grafts. Results have been variable and it is controversial whether these approaches provide long lasting solutions. It is also not sure whether these would not be accompanied by serious hazards such as the precipitation of nerve damage. Another interesting approach has sought to utilise challenge by BCG of sensitized subjects as a way to produce lymphokines for serving as a signal to macrophages for handling the intracellular bacteria (Convit **et al** 1974).

IV. **Preventive measures - Development of a vaccine :** The notion that there are indeed individuals with capacity to resist the disease stems primarily from epidemiological observations. It is noticed that in communities living in endemic areas, not all individuals develop the disease even though they are exposed to infection. An additional argument for the pertinence of the host immune system comes from the observed spectrum in which the disease is manifest. On one end of the spectrum is the lepromatous form of the disease in which the bacteria are seen proliferating abundantly. Infection is widely disseminated in contrast to the localization seen in tuberculoid leprosy. The subject in the latter case restricts the infection and is able to eliminate the bacteria. A challenge is thus posed : is it possible to improve the resistance of those subjects susceptible to develop lepromatous type of leprosy when infected ? Can the innate defence mechanisms be invigorated to counteract the infection ? One of the possible ways would be to develop a vaccine with capabilities better than BCG for improving the resistance to M. **leprae** infection.

The vaccine can be based on M. **leprae** antigens. This would however require the availability of the bacteria in large amounts initially for experimental purposes and subsequently for large scale production of an eventual vaccine. The source of the bacteria so far is by and large from human leproma biopsies which imposes immediately a serious limitation on the amount of bacteria procurable. The discovery of the nine banded armadillo as an animal capable of growing the bacteria is an interesting development (Kirchheimer and Storrs 1971). This animal is not native to India. Anteaters, lizards, snakes and other animals may be investigated as possible animals for growing this mycobacteria.

An alternate approach would be the use of cultivable mycobacteria with antigenic similarity to **M. leprae.** A number of saprophytic atypical mycobacteria have been isolated from humans. These could be screened for their potential to elicit immunity against **M. leprae.** The parameters to be borne in mind would be (i) antigenic cross reactivity, (ii) low potential for producing humoral antibody response, and (iii) high capacity to elicit cell mediated immune response.

The disciplines of Immunology, Biochemistry and Microbiology are developed to a high enough degree to accept the challenge, and given the right support, it should be possible to evolve better methods for control and prevention of this disease.

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Rehabilitation of Leprosy Patients*

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Rehabilitation in leprosy poses a major problem not only because of the disability caused by the deformities but also because of the fierce stigma attached to this disease. The leprosy patient is still not accepted in the programme for the rehabilitation of the other categories of the disabled and has to be treated apart from all other disabilities.

The era of rehabilitation in leprosy commenced only in the early fifties with attempts at surgical correction of the deformities. Although many procedures have been standardized for surgical correction much further work remains to be undertaken in this field based on the long term follow-up of the operated cases. Anaesthesia of the extermities and ulceration of the feet continue to pose a major problem in the rehabilitation.

Physical therapy in isolation or in conjunction with surgery has also proved its value in prevention and correction of the deformities.

Unfortunately all these advances have had little effect on the vocational rehabilitation of the patients. Most centres segregate the leprosy patients and provide such poor remuneration that the patients often prefer to take to alternate illicit and more remunerative occupations.

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*Abstract of the paper read at the symposium.

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President's Page

Greetings to Fellows and Members,

I wish to crave your indulgence for sending you this letter after four months of my taking over as the Presedent of the Academy. I had promised, at the time of my election, to write you as early as I could, and share with you some of the thoughts that have been engaging my mind about the future growth and development of the Academy. Permit me, at the out set, to express my deep appreciation and gratitude, for reposing your trust in me by electing me to the high office of the President. May I, as the first servant of your Academy, place before you some very urgent and important problems, which need your active cooperation, help and guidance, if we have to achieve their solution.

I have had a fair chance to get to grips with the problems of the Academy and the immediate task in front of us. The problems are many, but all difficulties must stimulate one to find a solution. The office of the Academy housed in a rented small flat of the All-India Institute of Medical Sciences needs considerable strengthening which in turn requires funds. The same applies to our immediate need to have a smoothly working infra-structure for the National Board of Examinations. Although the Union Government does provide some funds, yet these are quite insufficient and therefore, all of us have to make a joint effort to help with not only funds but also do our very best in raising standards—both professional and academic. All of us must now and again ask ourselves as to how much more can each one of us do to further the laudable cause for which we have founded the Academy. I do not need to remind you of the ideals and objectives we have set before us since you know them all.

The National Board of Examinations is going to hold the fourth series of examinations in August this year. The number of registrations for these examinations is increasing almost geometrically. The list of subjects in which the examination is conducted is also being enlarged. The Executive Director has already given you the details in the last issue of our Journal where he has also told you of our having acquired a plot of land next to the National Medical Library for putting up a building of the Academy. This is one of our immediate tasks and I would appeal to all of you to contribute your mite towards the building fund. The donations given to the Academy are exempted from income-tax. The building will have to be put up in phases. Prof. K. L. Wig, our past President, is the Chairman of the Building Committee. As the first step towards getting the project off the ground, namely collection of requisite funds, must be taken now, your help is urgently required. Not only does the Academy expect all its Fellows and Members to donate liberal funds personally but you are also requested to tackle all sources that are in a position to donate funds. You are the elite of the profession and therefore much is expected of you. You can send the donations to the Treasurer, Prof. Sanyal, with intimation to the Chairman of the Building Committee. I do wish to suggest that we donate one month's pay or emoluments for this purpose, in easy instalments, if we so desire.

I am writing to the State Governments also to help. Your help will also be required to pursue it with them.

The National Board of Examinations has the recognition of the Government and the M.A.M.S. qualification has been placed on the first schedule of the Medical Council of India Act, 1956. May I invite one and all of you to send me or to the Executive Director any suggestions you may have to improve the functioning of the Academy and/or the National Board of Examinations. I assure you I would greatly value such suggestions and would welcome them as index of your enthusiasm and wish to raise the dignity and academic standards of the profession to which we all have the privilege of belonging. The Academy is yours and in turn you all must build the Academy, into a national Institution which does credit to our ancient land and also to our profession, with a rich heritage going back to pre-Christian era of Gautam Buddha and Ashoka.

—P. N. CHHUTTANI

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Controller's Page

The MAMS Examinations were conducted in February, 1977 in the following subjects :—

I) **Basic Medical Sciences**

i) Pathology (Part-I)

II) **Medicine and Allied Sciences**

i) General Medicine	(Part-I and II)
ii) Pediatrics	(Part-I and II)
iii) Psychiatry	(Part-I and II)
iv) Radio-therapy	(Part-I)
v) Radio-diagnosis	(Part-I and II)
vi) Dermatology	(Part-I and II)

III) **Surgery and Allied Sciences**

i) General Surgery	(Part-I and II)
ii) Orthopaedics	(Part-I and II)
iii) Anaesthesiology	(Part-I and II)
iv) Obstt. & Gyn.	(Part-I and II)
v) Ophthalmology	(Part-I and II)
vi) Otorhinolaryngology	(Part-I and II)

IV) **Community Health**

i) Community Health	(Part-I)
ii) Integrated M.C.H.	(Part-II)
iii) Social & Preventive Medicine	(Part-II)

A total of 348 candidates appeared in Part-I and 77 in Part-II (theory). The results are as follows :—

PART-I

	Total Candidates appeared	*Passed*
Basic Medical Sciences	1	nil
Medicine and allied sciences	159	69
Surgery and allied sciences	178	66
Community Health	10	nil
	348	135

PART-II

	Total Candidates appeared	*Passed*
Medicine and allied sciences	35	12
Surgery and allied sciences	40	28
Community Health	2	nil
	77	40

Candidates appeared in 10 centres namely, Delhi, Bombay, Bangalore, Calcutta, Chandigarh, Jaipur, Lucknow, Hyderabad, Madras and Trivandrum.

Arrangements were also made to hold the Practical/Clinical Exams. at Delhi and Madras in the subject of General Surgery. A total of 14 candidates passed the theory examination in the subject.

The questions set contained papers of multiple choice questions (Part-I General Medicine) and a combination of short essay, multiple choice and essay type for the other subjects. The results were announced approximately one month after the theory examination. The following candidates passed in Part-I examinations :

MAMS (Part I) Examinations Result (February 1977)

I) Medicine and Allied Sciences

i) General Medicine

Total candidates appeared : 107
Total candidates passed : 49
Total percentage : 45.72

		Roll Number
1.	Dr. N. Karunakn Shetty, Mysore	Med/I/Bang/4
2.	Dr. Vishnu Mathur, Bombay	Med/I/Bomb/12
3.	Dr. Kanegaonkar V. Bhagwan, Sholapur	Med/I/Bomb/14
4.	Dr. R. R. Bhat, Bombay	Med/I/Bomb/15
5.	Dr. Vijay Mohan Rao, Calcutta	Med/ICal/16
6.	Dr. Manotosh Panja, Calcutta	Med/I/Cal/17

	Roll Number
7. Dr. Anjan Lal Datta, Calcutta	Med/I/Cal 18
8. Dr. Jayanta Kumar Basu, Calcutta	Med/I/Cal/20
9. Dr. Gautam Majumdar, Calcutta	Med/I/Cal/21
10. Dr. Subash Nandi, Calcutta	Med/I/Cal/26
11. Dr. Gursharan Singh, Faridkot	Med/I/Chan/32
12. Dr. Vibhay Bhatnagar, Chandigarh	Med I/Chan/33
13. Dr. S. S. Misra, Chandigarh	Med/I/Chan/38
14. Dr. Trivikram Shenoy, Chandigarh	Med/I/Chan/39
15. Dr. R. Harsha Rao, Delhi	Med/I/DH/49
16. Dr. V. Kumaraswami, Madras	Med I/DH/53
17. Dr. M. Chandrasekaran, Delhi	Med/I/DH/55
18. Dr. Satish Chander Gosain, Delhi	Med/I/DH/60
19. Dr. D. M. Abbey, Delhi	Med/I/DH/68
20. Dr. A. K. Agarwal, New Delhi	Med/I/DH/70
21. Dr. K. Rama Bala, Guntur	Med/I Hyd/76
22. Dr. S. M. Lal, Hyderabad	Med/I/Hyd 78
23. Dr. B. L. Choudhury, Jaipur	Med/I/Jaip/84
24. Dr. Hanuman Prasad Sharma, Bikaner	Med/I/Jaip/91
25. Dr. Deep Chandra Jain, Lucknow	Med/I/Luck/93
26. Dr. U. C. Goel, Lucknow	Med/I/Luck/98
27. Dr. Thomas Titus, Coimbatore	Med/I/Mad/100
28. Dr. S. Subhash Chandra Bose, Thanjavur	Med/I/Mad/101
29. Dr. T. Dhinkaran, Madurai	Med/I/Mad/102
30. Dr. J. Mohan Ashok Kumar, Alleppey	Med/I/Mad/103
31. Dr. Kuttappan M., Madurai	Med/I/Mad/104
32. Dr. S. Velumani, Madras	MedI/Mad/109
33. Dr. Mohideen Shaheed Jawahar, Madras	Med/I/Mad/112
34. Dr. B. Ramathilakam, Tanjore	Med/I/Mad/114
35. Dr. S. Sudershan, Madras	Med/I/Triv/117
36. Dr. S. Joseph Kutty, Trivandrum	Med/I/Triv/118
37. Dr. M. P. Divakaran, Trivandrum	Med/I/Triv/122
38. Dr. V. A. Rama Chandran, Trivandrum	Med/I/Triv/123
39. Dr. Suraraj Moni V., Trivandrum	Med/I/Triv/126
40. Dr. P. Vishwanathan, Trivandrum	Med/I/Triv/131
41. Dr. M. V. Imbichi Mammi, Trivandrum	Med/I/Triv/133
42. Dr. Joseph Varughese, Kottayam	Med/I/Triv/134
43. Dr. Vanchilingam, Thanjavur	Med/I/Triv 135
44. Dr. Gajendra Kumar Khatri, Chandigarh	Med/I/Chan/148

		Roll Number
45.	Dr. Vijay Raghwa Raa, New Delhi	Med/I/DH/150
46.	Dr. Dushrath Mal Bhandari, Delhi	Med/I/DH/151
47.	Dr. Sadasivan Jai Shankar, Delhi	Meh/I/DH/153
48.	Dr. Abhijit Chattarjee, Calcutta	Med/I/DH/156
49.	Dr. Bipin Behari Gupta, Delhi	Med/I/DH/158

ii) **Pediatrics**

1.	Dr. Philomena Pereira, Bangalore	Ped/I/Bang/2
2.	Dr. Mehta Rupa Ishwarbhai, Ahmedabad	Ped/I/Bomb/4
3.	Dr. K. H. Parmar, Poona	Ped/I/Bomb/5
4.	Dr. Bimal Kumar Kundu, Hoogly	Ped I Cal/7
5.	Dr. Krishna Kumar, Delhi	Ped/I/DH/11
6.	Dr. C. K. Sasidharan, Delhi	Ped/I/DH/13
7.	Dr. K. J. Poulose, Trivandrum	Ped I/Triv/27
8.	Dr. Susheela T. K., Trivandrum	Ped/I/Triv/29
9.	Dr. A. K. Kochar, Bombay	Ped/I/Bomb/32

iii) **Psychiatry**

1.	Dr. S. Devanathan, Bangalore	Psy I/Bang/2
2.	Dr. (Mrs)Ratna Bilwani, Delhi	Psy/I/DH/7
3.	Dr. N. Mathrubootham, Madras	Psy/I/Mad/10
4.	Dr. R. P. Rai, Madras	Psy/I/Mad/11
5.	Dr. M. R. Gopalkrishnan, Ernakulam	Psy/I/Triv/18

iv) **Dermatology**

1.	Dr. A. Mahakrishnan, Madras	Derm/I/Mad/12

v) **Radio-diagnosis**

1.	Dr. Roopa Chandan, Delhi	RD/I/DH/3
2.	Dr. Chaman Ram Soni, Palanpur	RD/I/Jaip/5
3.	Dr. V. L. Ratnakumari	RD/I/Triv/7

vi) **Radio-therapy**

1.	Dr. U. C. Pandey, Nainital	RT I/DH/2
2.	Dr. T. C. Nair, Trivandrum	RT/I/Triv/4

II. Surgery and Allied Sciences

i) General Surgery

		Roll Number
1.	Dr. B. S. Srinath, Simoga	Surg/I/Bang/6
2.	Dr. Edwin Ravi Kumar, Bangalore	Surg/I/Bang/8
3.	Dr. N. Prabhudev, Bangalore	Surg/I/Bang/12
4.	Dr. Shetty Sadanand, Bombay	Surg/I/Bomb/13
5.	Dr. Shivaji Basu, Calcutta	Surg/I/Cal/19
6.	Dr. Basant Kumar Gupta, C o 99 APO	Surg/I/Cal/20
7.	Dr. Tapan Kumar Banerjee, Howrah	SurgI/Cal 21
8.	Dr. R. S. Dhaliwal, Chandigarh	Surg IChan/25
9.	Dr. Satya Narayana Chary, Chandigarh	Surg/I/Chan/26
10.	Dr. Ishwar Prasad Goel, Delhi	Surg/I/DH/33
11.	Dr. Sharvan Kumar Gupta,Lucknow	Surg/I/Luck/56
12.	Dr. S. Nagarajan, Madras	Surg/I/Mad/59
13.	Dr. Daniel I Ananda Kumar, Madras	Surg/I/Mad/62
14.	Dr. K. V. Durai Raj, Madras	Surg/I/Mad/66
15.	Dr. R.C. Thamizhavell, Madras	Surg/I/Mad/68
16.	Dr. S. Manakavale Perumal Pillai, Madras	Surg/I/Mad/74
17.	Dr. K. Ramamoorthy, Madras	Surg/I/Mad/75
18.	Dr. Jagjeevan Ram, Madras	Surg/I/Mad/77
19.	Dr. Y. Achouba Singh, Pondicherry	Surg/I Mad/80
20.	Dr. M. D. Edward Ratna Kumar, Madras	Surg/I/Mad/81
21.	Dr. R. Venkata Gopala Krishnan, Madras	Surg/1/Mad/82
22.	Dr. P. T. Thomas, Kottayam	Surg/I/Triv/90
23.	Dr. S. Aravindaksha Kurup, Trivandrum	Surg/I/Triv/91
24.	Dr. J. Sivanandan Nair, Trivandrum	Surg I/Triv/93
25.	Dr. Abdul Kalam, Trivandrum	Surg/I/Triv/101
26.	Dr. Francia Cherian, Trivandrum	Surg/I/Triv/104
27.	Dr. Ramamurthy Ravi, Madras	Surg/I/Mad/105
28.	Dr. Vilas Deshpandey, Chandigarh	Surg/I/Chan/110

ii) Orthopaedics

1.	Dr. M. Mathew Issac, Vellore	Orth/I/Bang/1
2.	Dr. Nachinolcar Ulhas Gopal, Goa	Orth/I/Bomb/2
3.	Dr. David Rajan, Madras	Orth/I/Mad/8
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iii) Anaesthesiology

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3.	Dr. Malati Dattatrava Phadki, Delhi	Anaes/I/DH/18
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4.	Dr. V. Rajalakshmi, Madras	Obst/I/Mad 24
5.	Dr. S. Devambigai, Madras	Obst/I/Mad/25
6.	Dr. S. Padma, Madras	Obst/I Mad/26
7.	Dr. Maheshwari Ravi, Madras	Obst/I/Mad 31
8.	Dr. V. Rajasekharan Nair, Trivandrum	Obst I/Triv/34

v) E. N. T.

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Dr. K.S. Siddaraj, Bangalore	Med/II/Bang/22

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—N. JUNGALWALLA

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Ann Natl Acad Med Sci (India) 13, 3, July-September 1977

Obituary

Lt. Col. Jaswant Singh, FAMS

Lt. Col. Jaswant Singh, a founder Fellow of the National Academy of Medical Sciences (India), died on Sunday, the 13th February, 1977.

Col. Jaswant Singh was born on December 4, 1901 in Gujranwala, Punjab (now in Pakistan). He joined Indian Medical Service at the age of 26 after graduating in Medicine and Surgery from the University of Edinburgh. Four years later, he qualified for Diploma in Tropical Medicine and Hygiene from London. Subsequently, he received training in Malariology at the Malaria Institute of India, then at Karnal in 1934.

In 1938 he joined the Malaria Institute of India as a Research Officer and 9 years later he became the Director of the Institute. He made outstanding contributions in the field of immunology and chemotherapy of malaria. His early and active association with malaria control in Delhi city and rural areas in the country gave him the insight into organisational methods and administration which enabled him to launch National Malaria Control and Eradication Programmes in 1953/58 and National Filaria Control Programme in 1955.

During World War II, when malaria workers were faced with the acute shortage of Leishman and Giemsa stains, Jaswant Singh and his colleague L. M. Bhattacharji developed J. S. B. stain, which stands classified as one of the most efficient rapid water soluble stains and is widely used under National Malaria Eradication Programme in India and in countries of South East Asia.

During 1957, Col. Singh became the Director-General of Health Services. After his retirement, he served as Director of the W. H. O. Malaria Eradication Training Centre, Jamaica. He was associated with numerous scientific organisations in India and abroad. He was the Founder President of the Indian Society for Malaria and other Communicable Diseases. He was Editor of the Bulletin of the Society (now called Journal of Communicable Diseases) and the Indian Journal of Malariology. He was recipient of coveted Darling Prize for his outstanding contribution in the field of malaria.

Col. Singh is survived by his wife, two sons and a daughter. Fellows and Members of the Academy extend their deepest sympathy to the bereaved family.

Ann Natl Acad Med Sci (India), 13, 3, July—September 1977

Editorial*

Poliomyelitis in India

Poliomyelitis, an acute infectious disease caused by an enterovirus known as poliovirus with three distinct antigenic serotypes, type 1, type 2 and type 3, primarily affects the central nervous system of infants and children upto 5-8 years. The incubation period, on an average is 17 days. Primarily, poliomyelitis is an infection of the alimentary tract with the virus multiplying in the regional lymph nodes. There are no clinical manifestations unless the virus, after multiplying in the regional lymph nodes, passes into the blood stream and localises in the central nervous system. The anterior horn cells in the spinal cord bear the brunt of infection and depending upon the site and concentration of neuronal lesions, the corresponding musculature is paralysed. Rarely, cranial nerve nuclei or medullary centres are involved.

Only a small percentage of infected individuals suffer from a clinical disease and only in a minority there is paralysis or meningo-encephalitis. The patients with clinical manifestations of poliomyelitis represent merely the tip of an iceberg. There is no specific treatment for the paralysis produced by poliovirus. Apart from the general supportive measures, recommended in any acute infectious disease, **physiotherapy** in the affected limb offers the only respite. The paralysed muscle continues to recover for 1½-2 years beyond which there is not much significant recovery. The overall mortality is estimated to be low but owing to the social stigma attached to an individual with paralysed limbs education, employment and marriages do pose a social/rehabilitation problem for the society. Facilities for the laboratory diagnosis in a patient with an atypical clinical picture exist at the Post-graduate Institute of Medical Education and Research, Chandigarh ; Pasteur Institute of Southern India, Coonoor ; Virus Research Centre, Pune ; Haffkine Institute, Bombay ; Institute of Postgraduate Medical Education and Research, Calcutta ; ICMR Enterovirus Units at Ahmedabad and Nagpur, All-India Institute of Medical Sciences, New Delhi and the National Institute of Communicable Diseases in Delhi. The diagnosis is based on isolating the virus from patients' stool by inoculating the monkey kidney tissue cultures and observing any cytopathic effect attributable to poliovirus. A retrospective diagnosis is possible by demonstration of an increasing antibody titre in acute and convalescent phase sera.

Poliomyelitis occurs in India sporadically and epidemically (ICMR, 1977). Its incidence like, in other developing countries, is low in India. Improvement in living standards with reduction in spontaneous infection may paradoxically increase the incidence of more severe form of the disease due to lowering of acquired immune status due to sub-clinical infection. The age distribution of cases, like elsewhere may show a shift towards adolescents and adults. The serological investigations in different parts of country have indicated that the incidence of poliomyelitis is not dissimilar in rural, urban and remote hill areas (Pal et al, 1966 ; Bhatia and Gupta, 1968, Arya, 1976).

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*The views expressed in the editorial are the personal views of the writers and are not necessarily the views of the Academy.

Two types of prophylactic vaccines – the live attenuated and the killed are available for immunization. The killed vaccine has been used in experimental trials but has not yet been used in field trials ; oral live attenuated vaccine has been in extensive use in this country. The country depends for its supplies of oral poliovaccine on the Institute of Poliomyelitis, Moscow, USSR. The vaccine is imported as finished trivalent lots and in large quantities of the monovalent blends as well. From the monovalent blends, the Haffkine Institute, mix and bottle the trivalent vaccine in containers. The trivalent vaccine is imported and distributed through M/s. Spencer & Co. Unless the live vaccine is stored in sub-zero temperature, it looses its potency, and the use of such material gains little except a false sense of security. Loss of potency may occur during handling at any stage. In a study carried out by the National Institute of Communicable Diseases, Delhi, 191 samples were collected from 14 centres spread all over the country. It was surprising to note that in none of the centres there was any awareness of the effects of cycles of freezing and thawing. It was also revealed that importers and distributors were not handling the vaccine at subzero temperature. Only in 18 per cent of the centres deep-freez facilities were present ; in 60 per cent of the centres, the freezing chamber of refrigerators were being used ; in 20 per cent ordinary refrigeration and in rest none were used. The maintenance of vaccine was unsatisfactory in more than 60 per cent of the centres.

Of the total of 191 samples tested, there was no loss of potency in 113, marginal in 22 and marked in the rest. In the last category, destruction of vaccine was called for.

It is pleasing to note that authorities took early cognizance of the implication and have now made it obligatory for the main importers to distribute vaccine supplies in solid carbon dioxide. The regional and peripheral distributors have been recommended storage in deep-freeze. Further distribution may occur in dry ice or freezing mixture. A national monitoring system has been established to check the vaccine potency at the point of entry. The transport, storage and administration have been streamlined.

A constant vigil regarding the quality of vaccine at the administration point is imperative to ensure the success of the programme.

The sero-conversion rate with the live vaccine is lower in tropical countries (Lee **et al,** 1965). The presence of other interfering viruses in the gastro-intestinal tract, the depressant action of simultaneous administration of breast milk, potency deteriorations, presence of non-specific inhibitor in saliva and pharyngeal secretions (WHO, 1974) and malnutrition may be some of the many factors operative singly or in combination. This is an useful field of study for the researcher.

What is more needed is the realisation that to be effective strict compliance of rules regarding storage, distribution and administration is vital. Health education material on those have to be developed along with instructions in simple language for mothers, about what they should or should not do, so that full advantage of the programme accrues.

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—S.C. ARYA
—R.K. SANYAL

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Rehabilitation Past, Present and Future

B. Sankaran

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> "The lives of martyrs cannot be valued in terms of money. Their sacrifice is beyond recompense. But a grateful nation remembers its debt, and its obligation to mitigate the sufferings of their wives and children. Since our aim has been to give special help to the weakest in our society, at this moment we should not forget the other physically handicapped and disabled. They also need our help. Obviously, no society can afford to overlook its sick and handicapped"
> —INDIRA GANDHI.

Rehabilitation of the handicapped in India has been built into the culture in this country and in our society care for the handicapped and the diseased is as old as the **Vedas**. It would not be out of place to point out that the **Rigveda** compiled between 3500 to 1800 BC records the resuturing of a lacerated limb to enable the patient to walk. The Vanashadi Chandrodaya edited by Dr. C. Bhandari of Varanasi is a translation of the **Rigveda** mentions that the leg of queen Vishapala was amputated in a battle. After healing of the wound an iron leg was fitted to enable Queen Vishapala to walk and go to the battle field again. One wonders whether this was the first example of immediate post surgical fitting. The **Rigveda** records that the Ashwini Kumaras cured cases of paralysis and repaired successfully severely injured limbs. The growth of **Ayurveda** which was finally given the status of the Fifth Veda or **Pancham Veda** records treatment of leprosy with **Chalmugra** oil. The philosophy of Yoga and the teaching of certain postural exercises called **Asanas** for any part of the body was described in great detail and particularly exemplified in the classics of Charaka and Shusruta. Segrist a Swedish scholar in his History of Medicine states that this Yoga Asana stands competition with the best Swedish system. A surgeon of interest in Yoga is content at present and a proper evaluation and an attempt to successfully utilise it for purposes of rehabilitation is well accepted now. The value of pilichal and exercises and massages in the folkloric treatment of Kerala practised near Kozhikode is a continuation of the time honoured techniques of rendering help and exercises to the handicapped.

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*Shriram Memorial Oration delivered at the Annual Meeting of the Academy at New Delhi in January 1977.

**Director and Chairman.

The earliest instances of providing separate centre of living for the handicapped was predominant after the Ashokan era when he particularly established not only centres of Buddhism but also separate centres for the treatment and segregation of patients with leprosy.

Chandra Gupta Maurya the grand father of King Ashoka was the first one to recognise the importance of vocational training in the placement of the handicapped. He was responsible for opening of various centres throughout the country (Maurya Empire) where after defeat of the Kalinga Army the unfortunate defeated individuals who where limbless were provided with vocational training so that they could be gainfully employed. It is surprising however that all this glorious past had melted away and when independence came in 1947, centres of Rehabilitation in this country were indeed pitiably poor and a great deal had to be done in this specific field in this country.

The world at large did not however stand aside in the development of rehabilitation. Friedman in review of Amputations and Prosthesis in primitive cultures goes into great details about the existence of various figure heads particularly Mayan and Mexican culture approximately 1500—2000 years before the Christian Era in which various types of congenital amputations have been very clearly depicted. There is also evidence that the most common cause of amputations in this Era of Pottery was traumatic, medical and punitive. An Italian Vase of the 4th century B. C. shows a lame walking with a rod an original pylon and a mosaic in the Cathedral of Lescar shows a black walking with a wooden pylon leg very similar to what is being used today. In Capua in Italy in 1858 two stones of the third century B.C. were discovered in which archeological evidence of a prosthesis in bronze, iron and wood had been demonstrated. This prosthesis was preserved in the the British Museum in London but unfortunately was destroyed during an air raid in 1941.

History also records that Marcus Sergius a Roman General had lost his right hand in the second Punic War 218 - 202 B.C. and was fitted with an iron hand which he used very effectively. Amrosi Parre designed an artificial hand called lepetit Lorrain with a fixed thumb and with spring loaded moveable fingers. He also devised an above knee prosthesis with external locking knee joint that could be released by a gatch running from the hip. One of the first persons to use shoulder and trunk muscles as a source of external power to flex and extend the fingers was by a German dentist Peter Balliff. In 1844 a Dutch sculptor devised such a prosthesis and in addition he was also able to flex the elbow using his shoulder girdle muscles. The first person to use a suction socket for both arm and legs was Dubois Parmalle who invented it in 1863 though it came to general acceptance only 90 years later. Probably the custom of cremation of the dead in this country might have resulted in substitution of human limbs in our country having gone unrecorded. Professor Ernest Marquardt has quoted a drawing of a Swedish amelic of 1654 who was totally rehabilitated and was able to utilise her feet for all her daily activities including eating, sewing, cooking and caring for a child. It is quite common to see bilateral amputees of the upper extremity or a child of bilateral limb deficiency utilising this technique for daily activities. Fortunately we were spared of the thalidemide disaster which in many countries produced a large number of alemic extremities.

Growth of rehabilitation services in this country in the last 30 years since Independence has been progressively rapid and we can state with some confidence that within the next few years we would have reached delivery of such services to the outer most periphrey. The first centre of Rehabilitation was associated with the Armed Forces. It was originally set up in 1942 at Sialkot but within a short time this centre was moved to Poona where it grew into a large artificial limb centre which has served the needy and the handicapped for many years and has served well the Armed forces during the 1962, '65 and '71 operations. The Poona centre has in addition got ancillary facilities which are provided by the 515 Army base workshop which produces component parts and corresponding rehabilitation facilities are available at the Army Medical Rehabilitation Unit Kirkee, the Spinal Injury Unit at Kirkee for vocational rehabilitation. The Armed forces have also served their amputees and the handicapped by providing them vehicle transport, vocational placement centres and sub-centres for repair of limbs have been located in their other Command Hospitals as in Lucknow, Secunderabad, Madras and at other locations. The basic educational aspect of the entire Armed Forces programme has been primarily that of inservice apprenticeship training and because of the Motto of the Armed Forces to never let any of its men down adequate employment opportunities have been provided for all the handicapped particularly those who had injuries as a result of injury in the battle field.

In 1947 the first Society for the Rehabilitation of the Crippled Children was started in Bombay due to the efforts of late Dr. M. G. Kini and Mrs Fatima Ismail. This Society was responsible for the running of a hospital and a child care rehabilitation centre which later on formed one of the nucleus of the All-India Institute of Physical Medicine Rehabilitation, Bombay. Bombay as in many other fields of medicine has led the country in the field of rehabilitation as well. In 1950 at the K.E.M. Hospital the WHO started a rehabilitation department and Mrs Nimbkar established the First Occupational therapy school in the country in 1950. In 1953 the First Physiotherapy school was started. Mrs Nimbkar's activities spread to Nagpur where she was responsible for the establishment of the Nagpur Regional centre called NORCOD. In 1955 the U. N. Rehabilitation project jointly sponsored by the Government of India, Bombay Muncipal Corporation, the United Nations and the World Veterans Federation brought into being the All-India Institute of Physical Medicine Rehabilitation which ultimately was to become a pioneer centre in this particular field for a number of years. It was headed by late Dr. M. V. Sant whose dedication and undivided attention and loyalty was responsible for the growth of the institution to an excellent centre of training and rehabilitation of the handicapped, vocational counselling, social rehabilitation, physio-occupational therapy and other aspects of rehabilitation. Bombay in addition has a very large centre in the Federation of the Physically handicapped which is well motivated and runs a centre for providing employment opportunities to the physically handicapped.

In the last 15 years rapid strides have been made in the establishment of multiple centres and many of these centres came up with the help of the social rehabilitation services in Washington D.C. These include centres of excellence in Madras, Vellore, Bangalore, Trivandrum, Miraj, Calcutta, A.I.I.M.S., New Delhi and at Ludhiana. These centres which grew primarily as research and development centres in field of the rehabilitation have assumed the role of leaders in the field and are able to deliver good rehabilitation services to the various parts of the country. The Central Institute of Orthopaedics established in 1961 in the Safdarjang Hospital, New Delhi had rudiments of excellent rehabilitation centre which has now flowered into a full scale Department of Rehabilitation with all modalities of rehabilitation well established. Unfortunately a very large lacuna existed in many parts of the country particularly in the areas of the most popular states of U.P., M.P., Bihar and Orissa as also Andhra Pradesh. In addition the centres at Jabalpur, Patiala, Patna and Lucknow needed further strengthening and it became apparent that all these would be possible only if a National Scheme of Rehabilitation is conceived and worked out.

Unfortunately the trend today is primarily concentration of provision of services to the physically handicapped and a large lacuna exists in the field of the mentally retarded. Rehabilitation of the blind has very fortunately being very actively worked upon by the All India Society for the Prevention of Blindness and a National Programme for blind rehabilitation had become ready for the Vth Plan period. The deaf and other varieties of the handicapped are still to find their place in Society and efforts like establishment of Logopedic Institute at Bangalore have touched only the fringe of the problem.

The untiring and unstinted efforts of Mrs. Karan Singh and Mrs. Vasanti Pai have been responsible for the elevation of services of the mentally retarded to a greater level of importance and with a larger emphasis placed on this specific aspect of rehabilitation of the mentally retarded I believe we would be able to get somewhere in the near future.

I have till now specifically not mentioned the creation of the Artificial Limbs Manufacturing Corporation of India which has been established by the Government, Ministry of Industry for the purposes of providing component parts and artificial limbs and the establishment of 32 regional and peripheral limb fitting centres throughout the country so that there could be an equivable distribution of services particularly at the periphery. The ALIMCO as the Corporation is called, was started in 1973 has now grown in size to a capacity capable of production and has been able to satisfy the needs of its own regional and peripheral limb centres immediately and also been able to produce export quality products to certain specific countries. The growth of this Company would be watched with considerable interest since there has been a large amount of input into this centre and the centre is hoped to provide necessary facilities of rehabilitation to physically handicapped on a much larger scale with more sophisticated products which persons in this country could afford.

While we have been making this attempt in the last 25 years very marked and rapid strides have been made in the field in the rest of the world and the gap that existed in 1947 which probably could be about 15 to 20 years has increased enormously in the last two decades. We have a great deal to catch up with the rest of the world in the succeeding years if we have to maintain expertise in the field and also keep our perspective clear and make services to the handicapped available on a much wider scale and also keep pace with the rest of the world.

The wheels of progress keep turning and there is never an end to the listing of horizons of providing the ultimate scientific aids to the field of the handicapped. Man today is faced with a general shortage of energy. The world has adequate energy and it is only a question how to harness and distribute it effectively for the benefit of all. That is the burning question of day. Solution for this matter is extremely important because it involves humanity's long term survival. The neuromuscular handicapped who has to be motivated and locomotised maximum utilisation of energy finds the energy crises is deeper concern because for him energy is vital for survival.

All human beings are handicaped to various relative degrees. I do not believe there is a single individual who does not possess some handicap or the other. Fortunately a large amount of us have such trivial handicaps that we are able to overcome them with adjustments in our life. For paraplegics to be able to ambulate and to go to work in a transport which he can drive and get into so that he could take care of his own self in life is not a dream but a matter of daily sustenance. Unfortunately in our country this is not possible except for a very small proportion. The possibilities of providing controlised energy source outside to ambulate this man is a distinct possibility with a battery operated wheel chair. It has now been possible to even produce locomotive devices for the high quadraplegia and could we imagine that one of the most suitable methods of locomotion for the human beings of high level quadraplegia is lunar rover vehicle that was originally designed for transport of man on Moon. The possibilities of utilisation of the vehicle without much energy expenditure and its general utility in soil of all types show the extent to which in the space age has become applicable to the field of rehabilitation. Similarly spectacular progress has been made in the use of external energy for the rehabilitation of the neuro muscular patient, with energised legs and arms and probably even spinal cord injury patients. These were science fiction of yesterday and already seems possible within the next few years. The functional electrical stimulation of a hemiplegic gait has now become a reality for functional electric stimulation of the detrusor of the bladder with electronic stimulators implanted in the conus medularis activated by radio signals from the bladder has become a distinct possibility and electricity have given a great deal of expandable air energy in the field of rehabilitation of the handicapped is particularly true in upper limb prosthesis and orthosis. One of the most important lacuna that exists is a feed back system from a prosthesis like device to a patient that he could perceive what he feels at the end of the limb. Implantable electrodes in the stumps and electro myographic signals which can readily be interpreted are only the beginning in this field. An electro cutaneous feed back of the skin has been the subject of detailed study and this has been made possible by providing sensory devices which are primarily pressure transducer at the end of the artificial limb devices by use of micro switches and micro circuits. Probably this type of a device would ultimately be useful in the whole arm brachial plexus palsy where loss of sensation makes the limb a useless burden on the patient.

Till now we have primarily concentrated on the amputee. The blind has been rehabilitated with the use of a long cane. But a Thypholo cane with electronic input has become a distinct possibility. The Laser cane with specific property of guiding the blind person in different areas curves up and down stairs or in crowded streets has become a distinct possibility in the last few years. Introduction of the Laser cane is now on a purely experimental basis and has to be adequately evaluated for daily use. Visual feed back system for reading machines for the blind using normal script and print and stimulation devices to arouse sensory devices which would indicate presence of barriers have recently been developed and the entire scope of rehabilitation of the blind within the next few years would be an eye opener to many in the field.

Critical areas still exist where much work needs to be done and this is particularly true in the field of the mentally retarded where communication gaps exist between parent and the child and the teacher and the taught. The recently introduced Bliss system primarily dealing with symbols has found general acceptability in certain centres of the world particularly in Australia and Canada provided a glimmer of hope to these unfortunate individuals.

We must remember that mentally retarded are no small in number and they would continue to increase if we do not make serious attempts of preventing this disability by various steps. We do know that there is a large amount of genetic transmission and genetic counsel before marriages are undertaken particularly consangunity is a common institution in our country. Similarly avoidable RH and compatabilities must be strongly emphasised since frequently these produce a great disaster. Similarly many other mentally retarded families can be prevented particularly Mongolism and other genetically transmitted diseases and congenital anamolies are present. Inspite of all these attempts are prevention of this disability system of communication must be evolved.

This series of symbols which primarily today is an experimental stage and is at present primarily utilised for communication between groups of children has now been put on a computer board so that children could speak with each other to their parents and teachers. Probably this language of symbols is the language of peace as Bliss hopefully puts it.

Lastly a great deal of work still needs to be done in the field of vocational placement of the physically handicapped and the mentally retarded. We have made practically no progress in this field. Indeed we have even fallen back from the Maurya edict which had certain code of conduct for the establishment of centres for these unfortunate individuals. Necessity for legislation for utilising the services of the handicapped on a large scale has to be evolved if we are able to break some of the fundamental barriers which we have artificially created in this field.

Recently there has been an examination of the reactions of a family to the arrival of a handicapped child. I think this represents the reaction of an Indian community as well. The process consists of four original phases – denial, guilt, projection and dependency. Denial comes early. It is a defensive reaction and the family refuses to believe the bad news and the community responds in the field of the mentally retarded. Community pities the family but does no more than that. There is even a feeling on the part of the community to disregard the family's difficulties and problems. Most often in our set up the mother of the child is the one of derision and laughter and sometimes the child with the matter is packed back home of her parents. If the family accepts responsibility to treat the child it goes through a process of denial conducting the poor child on expeditions to various physicians and advice from lay men and ulimately finds an individual who would deny existence of the problem and assures them that no handicaps exist.

Our society lends a deaf ear to the problem. The problem of guilt is primarily that of the parents and guilt factor might be responsible for denial of a rightful place for the child in its environment. The guilt reaction is communicated to the child in the form of a tedious explanation or an attempt to protect the child from a mental assault and frequently this guilt reaction leaves a depression to both the parents and is communicated to the child by the sub conscious. The child thus becomes irresponsible and therefore further loses the sympathy of the mother as well as the community. Projection is normally an attempt on the part of the parents to blame another individual or doctor and this is particularly true in the cerebral palsy child.

Dependency which finally occurs in many families and communities is the process of adaptation of difficulties the child faces which should not be out of pity but out of significant desire of the family to help the child. It should never be overdone or underdone. Such a well thought out process of integration hopefully serves the handicapped. We sincerely hope we would be able to bring this process to fruition in the succeeding years so that atleast in another 10 years time we may have caught up with the 30 odd years development at gap that presently exists in this specific field.

I would like here to enlighten the audience on the spirit of this Decade of Rehabilitation. The International Society for the Rehabilitation of the Disabled decided to declare the 70s as a decade where the problems of the handicapped will figure in the minds of many governments. We are happy that in India this decade has meant a new era in the field. The genuine goals of this decade are : (1) To awaken the increased public interest in the growing dimensions of the problem of disability in all countries and in the economic and social advantages of providing adequate services ; (2) To encourage governments to give a higher priority to the problems of disability and to make necessary budgetary allocations for their part in their solution ; (3) To make available to the countries needing it guidance in planning and developing rehabilitation services ; (4) To increase in volume and accelerate in pace the training of professional and auxillary personnel needed to man rehabilitation facilities ; and (5) To develop methods and procedures which will facilitate the delivery of more service to larger numbers of persons at lower cost in personnel time and in other scarce resources.

Finally I would like to end my memorial oration with a quotation from the Hon'ble Prime Minister ; "For the brave young men, straight and strong in body to be suddenly without a limb is not only a matter of physical pain but of mental shock and agony. None of these want pity or charity. What they need is compassion, understanding and assistance to readjust themselves to the sudden and unforeseen change in their lives. We must assure them that life still has much to offer them and they in turn have much to offer society." And one from Late Martin Luther King : "I have a dream that one day every valley shall be exalted every hill and mountain shall be made low the ronger places will be made plane the rooked places will be made straight and the glory of the Lord shall be revealed and all flesh shall see it together. Let this not remain a dream for the handicapped but a fulfilment...."

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Pharmaco-therapeutic Investigation on some Medicinal Plants

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Introduction

Since ages plants and their extracts have been used for the cure of localized and generalized human infections by the common folk. A number of surveys have been carried out by various workers pointing out the wide distribution of anthelmintic, antibiotic principles in higher plants. Osborn (1943) states that little attention seems to have been paid either to the selection of herbal flora, in relation to its alleged medicinal properties or to the use of those test organisms which are essentially disease producing organisms. At the same time no effort seems to have been made to separate the real useful one from others.

Carpenter (1945), Omer (1945), Toropzev and Kamner (1946), Rao **et al** (1946a) Rao **et al** (1946b), Dutta **et al** (1947), Ikram (1972) and Zofia and Zofia (1973) have well documented the the antibacterial and antifungal activity of **Allium sativum Linn.** Sanfiilppo and Ottaviano (1944), Enrique (1946) and Chopra **et al** (1955 and 1958) have studied the active principle of **A. sativum** for its other pharmacological activities, on isolated heart, intestine and on the blood pressure of cat.

Ikram (1972) and Bhatnagar-Thomas and Pal (1974) have also indicated its insecticidal and anticholinesterase activity. But no attention seems to have been paid to rule out its irritant activity.

Nadkarni (1954a, b) and Chopra **et al** (1958a) indicated the antiseptic **Balsamodendron mukul Hook,** activity of Mehta **et al** (1968) demonstrated the effect of **B. mukul** in case of hypercholestraemic in chicks but its systematic antibacterial and pharmacological activities have no where been indicated.

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*Part of the work of the thesis submitted by the senior author in partial fulfilment of the requirements for the M.V.Sc. degree in Pharmacology of the University of Agra.

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Nadkarni (1954), Chopra and Chopra (1955b), Chopra **et al** (1956b) and Sharma **et al** (1967) indicated the anthelmintic activity of **V. anthelmintica Wild.** From this it appears that no systematic anthelmintic or antibacterial activity has been made available along with pharmacological activities.

Hence for the present investigation of indigenous Indian plants, "**Allium sativum Linn (Bulbs), Balsamodondron mukul Hook (Oleo gum resin) and vernonia anthelmintica Wild (seeds)**", have been considered worthwhile to investigate their anthelmintic and antibacterial effect ruling out their side effect limiting their use.

Material and Methods

1. **Anthelmintic activity :** Anthelmintic activity of **A. sativum, B. mukul** and **V. Anthelmintica in vitro** were carried out on the mature and actively motile **Ascaridia galli** worms as described by Sharma **et al** (1967).

2. **Antibacterial activity** : Antibacterial activity was assessed by cup-plate method, using the **B. subtilis** as gram positive and **E. coli** as gram negative organisms.

3. **Esterification and Amination process :** The irritant effect of ether extract (active principle) of **A. sativum** was ruled out by preparing ethyl ester as per the method by Dean (1921) and by treating the ether extract with ammonia as well, but the anti-bacterial effect was also lost, hence no further effort was made in this direction.

Pharmacological activities Part-I

In vitro studies were carried out with different extracts of **A. sativum, B. mukul** and **V. anthelmintica** to find out their effects on isolated guinea pig ileum, rabbit jejunum, rat ileium, rat uterus, perfusion of frog's heart, perfusion of rabbit's heart and anticholinesterase activities.

Pharmacological activities (in vivo)

The effect of **A. sativum, B. mukul** and **V. anthelmintica** were studied on blood pressure and respiration of anaesthetised dogs pentobarbitone sodium 40 mg./kg. intraperitoneally. Studies to find out the local anaesthetic effect of colloidal solution of **B. mukul** were carried out as per the method described by Bulbring and Wajda (1945).

Therapeutic trial : Therapeutic trial was conducted in mice infected with staphylococcus aureus and **E. coli.**

Results and Discussion

Though antibacterial activity of **A. sativum**, has been worked out by various workers, Carpenter (1945), Omer (1945), Toropzev and Kamner (1946), Rao **et al** (1946a) Rao **et al** (1946b) and Datta **et al** (1947) and is well documented ; but no attention seems to have been paid to rule out its irritant effect limiting its use. From the trials to rule out its irritant activity either by esterification or by treating the ether extract with ammonia, showed that these methods did abolish its irritant activity but its antibacterial activity was also lost.

Sanfiilppo and Ottaviano (1944) investigated the pharmacological properties of **A. sativum** on rabbit, guinea pig and dog with regard to arterial pressure and respiration. Enrique (1946) described the pharmacological action of the active fraction on isolated frog heart, isolated rabbit heart, intestine and anaesthetized cats, and indicated atonic effect on heart, the paralysing effect on isolated rabbit intestine and slightly hypertensive effect on anaesthetized cats, which has, however, been not confirmed, at the dose mentioned earlier, during the present investigation.

Chandorkar and Jain (1974) too indicated the stimulant activity of garlic on isolated rabbit hearts which has not been observed during the present study. During this study (Fig. 4A and 4B, Plate II) its activity to cause stimulation of isolated rabbit heart could not be confirmed. The ether extract rather caused a delayed type of negative chronotropic and negative ionotropic effect when used at the dose of one mg, was blocked by atropine. No tachyphylaxis was observed. The effect was also not altered by bunalol or hexamethonium or by pretreatment with reserpine. From this it appears that the cardiac effect may be due to vagal stimulation.

Ether extract **A. sativum** did not show any marked effect on the motility of **A. galli** worm studies **in vitro**. Hence it can be said that the reputed anthelmintic activity of **A. sativum** by the common folk is not beyond doubts.

Though **B. mukul** has been indicated as an antiseptic by Nadkarni (1954) and Chopra **et al** (1958a) but during the present investigation no such marked antibacterial activity of colloidal solution of **B. mukul** used could be shown against **B. subtilis** and **E. coli** as gram positive and gram negative organisms respectively. Hence its use as an antiseptic in various conditions like ulceration, bronchitis, pneumonia, pyelitis, cystitis, leprosy, syphylitic and tuberculosis advocated by Nadkarni (1954a, b) and Chopra **et al** (1958a) can not be supported. Its activity in induced hypercholestraemia in chicks has been described by Mehta **et al** (1968). But its general pharmacological screening has no where been found. During the present investigation colloidal solution (Singh, 1973) of **B. mukul** could cause a non-specific antagonism to histamine, acetylcholine and nicotine (Fig. 1 Plate I) and rabbit jejunum (Fig. 3 Plate I).

On isolated frog heart it could cause negative inotropic effect which was not blocked by atropine but did not produce any effect on isolated rabbit heart. From the study carried out it is clear that it does not have any anticholinestrase activity as well.

Its effect on the A. **galli** worms is also not indicative of its anthelmintic activity.

The activity of the colloidal solution of **B. mukul** used at the dose of one mg/kg., 10 mg/kg. and 100 mg./kg., body weight could not cause any protection against the MLD of gram positive (staphylococcus aureus) and gram negative (E. coli) organisms **in vivo.**

Its action as uterine stimulant indicated by Nadkarni (1954) could not be ascertained during the present investigation.

V. anthelmintica has been reported as anthelmintic by Nadkarni (1954), Chopra **et al** (1955b), Chopra **et al** (1956b) and Sharma **et al** (1967). But during the present studies anthelmintic activity of **V. anthelmintica** could not be confirmed even upto the dose of 100/μg./ml.

The studies carried out with the active bitter principle of **V. anthelmintica** also did not show any antibacterial activity.

On the guinea pig ileum it could antagonise only the spasmogenic action of histamine (Fig. 2) but not of acetylcholine, barium chloride and nicotine. Similarly on dog blood pressure it could reduce the vasodepressor response of intravenously injected histamine (1 μg./kg. body weight).

From this it appears that active bitter principle of **V. anthelmintica** might be a true antihistamine, blocking the effect of H_1 receptors completely while blocking the effect of histamine partially on cardiovascular system of dog.

Conclusion

From the present study it appears that none of the three indigenous Indian drugs studied A. **sativum, linn, B. mukul Hook** and **V. anthelmintica wild** possess any anthelmintic activity, though **A. sativum** possess high antibacterial activity but it can not be used parenterally due to its irritant effect which could not be ruled out.

B. mukul though showed an insignificant antibacterial activity but is of little use therapeutically.

PLATE I

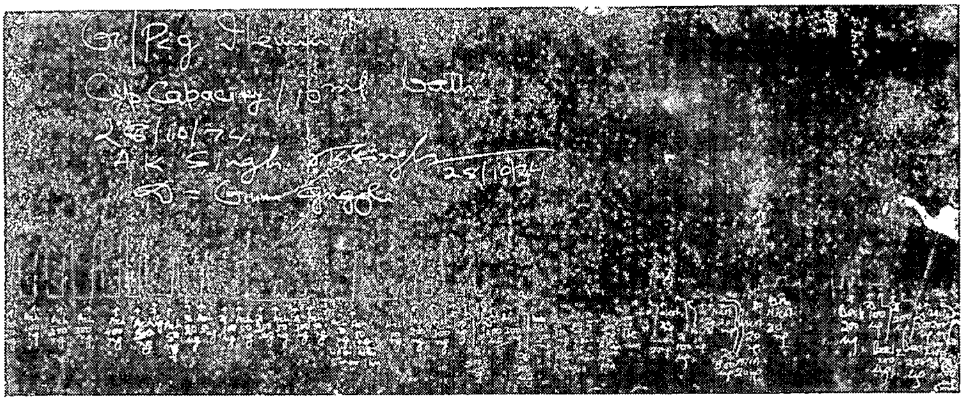


Fig. 1

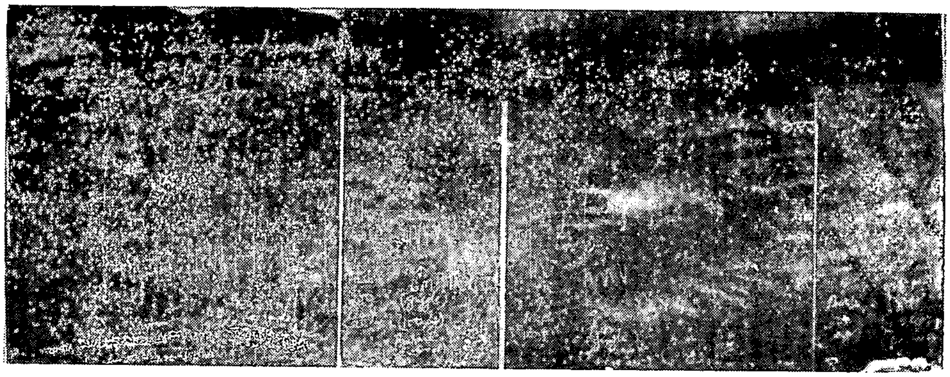
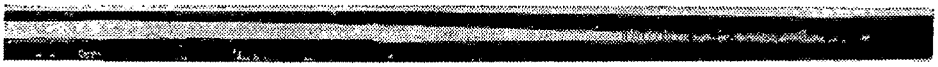


Fig. 3

PLATE II

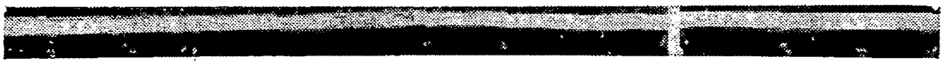
ISOLATED RABBIT HEART

Figure 4A



A_1=Allium Sativum Linn (Ether Extract)

Figure 4B



A_2=Allium Sativum Linn (Aquous Extract) G=B Mukul Hook (Gum Gugul)

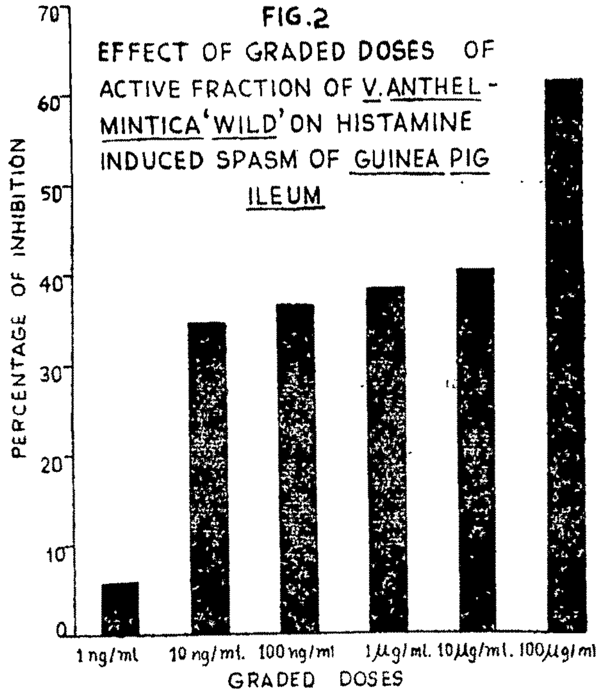


FIG.2
EFFECT OF GRADED DOSES OF ACTIVE FRACTION OF V. ANTHELMINTICA 'WILD' ON HISTAMINE INDUCED SPASM OF GUINEA PIG ILEUM

V. **anthelmintica** has shown quite encouraging antihistaminic activity requiring further evaluation.

Acknowledgment

The authors are grateful to Dr. C.M. Singh, Director, I.V.R.I., Izatnagar for the facilities afforded for the work.

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Influence of Body-weight on Blood Pressure in an Adult Rural Population

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An investigation of casual blood-pressure, covering 1,325 individuals, aged 15 years and above, was carried-out by door to door visit, in 5 villages of Jhansi district, U.P., with the objective to study the influence of body-weight on blood pressure levels. A tendency of significant increase in the quantum of both pressures, systolic as well as diastolic, with advancing weight was observed in both males and females. However, the extent of relationship of systolic and diastolic blood pressure levels with body-weight did not differ significantly ($P > 0.05$) in the two sexes.

Introduction

Blood pressure of an individual, in view of redundancy of numerous publications on the subject, has been a matter of wide discussion. Multifactorial dependence of blood pressure has widely been realized and various personal and environmental factors **viz.** psychological-stress (Henry and cassel 1969; Leigh 1971), heredity (Pickering 1967, Platt, 1967), age and sex (Indrayan and cassel 1972a, Gordon 1964) body-built (Sive **et al** 1970) and social-status (Indrayan **et al** 1972b) have been discussed and broughtout as blood pressure correlates. Some attempts (Miall **et al** 1968, Florey and Acheson 1969) have also been made to explain the influence of weight on systolic and diastolic levels of blood pressure. But in India, especially for rural inhabitants, a little attention seems to have been devoted to define the significance of weight on blood pressure levels. An investigation, under domiciliary conditions, was undertaken in an adult rural population with the objective to study the influence of weight on blood pressure levels.

Many authors, while discussing the significance of some of the blood pressure correlates on its distribution, have often used mean and standard-deviation to represent the characteristics of blood pressure distribution, which may, however,

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***Demonstrator.

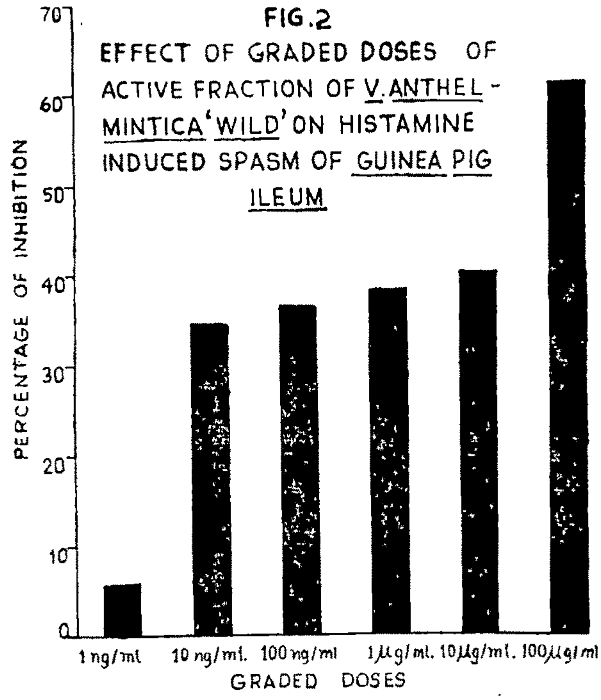

FIG.2 EFFECT OF GRADED DOSES OF ACTIVE FRACTION OF V.ANTHELMINTICA 'WILD' ON HISTAMINE INDUCED SPASM OF GUINEA PIG ILEUM

V. anthelmintica has shown quite encouraging antihistaminic activity requiring further evaluation.

Acknowledgment

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Influence of Body-weight on Blood Pressure in an Adult Rural Population

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An investigation of casual blood-pressure, covering 1,325 individuals, aged 15 years and above, was carried-out by door to door visit, in 5 villages of Jhansi district, U.P., with the objective to study the influence of body-weight on blood pressure levels. A tendency of significant increase in the quantum of both pressures, systolic as well as diastolic, with advancing weight was observed in both males and females. However, the extent of relationship of systolic and diastolic blood pressure levels with body-weight did not differ significantly ($P > 0.05$) in the two sexes.

Introduction

Blood pressure of an individual, in view of redundancy of numerous publications on the subject, has been a matter of wide discussion. Multifactorial dependence of blood pressure has widely been realized and various personal and environmental factors **viz.** psychological-stress (Henry and cassel 1969; Leigh 1971), heredity (Pickering 1967, Platt, 1967), age and sex (Indrayan and cassel 1972a, Gordon 1964) body-built (Sive **et al** 1970) and social-status (Indrayan **et al** 1972b) have been discussed and broughtout as blood pressure correlates. Some attempts (Miall **et al** 1968, Florey and Acheson 1969) have also been made to explain the influence of weight on systolic and diastolic levels of blood pressure. But in India, especially for rural inhabitants, a little attention seems to have been devoted to define the significance of weight on blood pressure levels. An investigation, under domiciliary conditions, was undertaken in an adult rural population with the objective to study the influence of weight on blood pressure levels.

Many authors, while discussing the significance of some of the blood pressure correlates on its distribution, have often used mean and standard-deviation to represent the characteristics of blood pressure distribution, which may, however, sometimes fail to reveal the picture in its totality. Acheson (1973) has suggested for carrying-out the percentile analysis of the blood pressure distribution for depth study. Holland (1963) called mean and standard-deviation of means as crude measures to compare the blood pressure of two or more groups and has recommended for the presentation of full frequency curves. W.H.O. Expert Committees on Hypertension and Coronary Heart Disease (1959), and Epidemiological Methods in the Study of Chronic Diseases (1967), have also urged for the presentation of full distribution curves of blood pressure measurements wherever possible. This paper, beside regression-analysis, presents percentiles of systolic as well as diastolic levels of blood pressure by weight and sex alongwith full distribution curves.

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Material and Methods

The present study is the cross-sectional survey of casual blood pressure of the individuals, aged 15 years and above, in 5 villages **viz.** Kochha Bhanwar, Kargavan, Pichhore, Digara and Mary, lying within the radius of 8 kms. from the head-quarters of Primary Health Centre, Kochha Bhanwar, district Jhansi, U.P. The study sample included 2, 212 individuals in 665 families but blood pressure along with weight could be recorded for 1,325 (59.9 per cent) individuals and rest 887 (40.1 per cent) could not be contacted due to either their continual absence or non co-operation.

The survey was carried-out during the year 1972 between 7 A. M. and 12 Noon by the medical Interns, trained before hand for the purpose. Blood pressure readings were taken on the left arm with the respondent sitting in their own domiciles, their natural nestling place, with mercury sphygmomanometer applying auscultatory method, detailed by American Heart Association (1951). Readings were made to the nearest 2 mm. Hg. To stave-off the possible fluctuations, three consecutive readings were recorded for both the pressures and the average of these three readings has been utilized in subsequent analysis. Both, systolic as well as diastolic readings, were divided into 10 mm. Hg. groups as recommended by Borhani **et al** (1969) in order to eliminate the effect of digit preference, if any. Besides the considerable limitations of casual blood pressure, only such pressure could be taken due to the obvious reasons (Davies and Lewist, 1966).

Weight was recorded with the respondent standing on adult weighing machine, without support, pockets emptied, without shoes, and wearing knee-length least possible clothes. Regression-analysis was carried-out on the points suggested by Kapoor and Saxena (1963) and significance of the differences were worked-out by utilizing the statistical techniques available (Kapoor and Saxena, 1963).

Results

Percentage-distributions of both the pressures, systolic as well as diastolic, for each 10 kgs. weight-groups for males and females separately have been presented in graphic forms (Figs. 1 and 2) and corresponding mean blood pressure levels along with standard deviations have been shown in Table I. The distributions, in each case, revealed some trends not only in respect of means but in respect of other characteristics as well. Following observations may be made :

(i) The dispersion of systolic blood-pressure in both the sexes, was higher than diastolic for each weight-group indicating relatively greater inter-individual variability of systolic than diastolic level of blood pressure for each weight-group in both the sexes.

(ii) Slight shifting of the distributions to the right with advancing weight, in each case except in systolic blood pressure for females, indicated some rise in the blood pressure levels with increase in weight. For females, distributions of systolic pressure also shifted to the right for each weight-group except the weight-group 30-40 kg. which implied some enhancement in the systolic blood pressure with weight for females heavier than 40 kgs.

(iii) A tendency of positive skewing with advancing weight indicated that persons with raised level of blood-pressure amongst heavier weight-groups were more than expected and thus suggested increasing impact of weight in raising the level in these weight-groups.

In order to have a deeper probe into the relationship of blood pressure with body-weight, percentiles of both pressures, systolic and diastolic by weight for both males and females were worked-out and have been presented in Tables II to V and depicted in Figs. 3 and 4 respectively.

It was of interest to note that mean levels (Figs. 3 and 4), shown by crosses were a little higher than corresponding medians which is a heavy line in each figure. This indicated for the right skewing of the frequency curves in each case. The relatively lesser differences between mean and median blood pressure levels in case of diastolic than systolic for both the sexes indicated comparatively lesser degree of skewness in diastolic than systolic level of blood pressure.

Another characteristic of the distributions that was less likely to be due to the sampling variations, was a considerably different configuration of higher percentiles

Graph showing percentage distribution of systolic and diastolic blood pressure in males

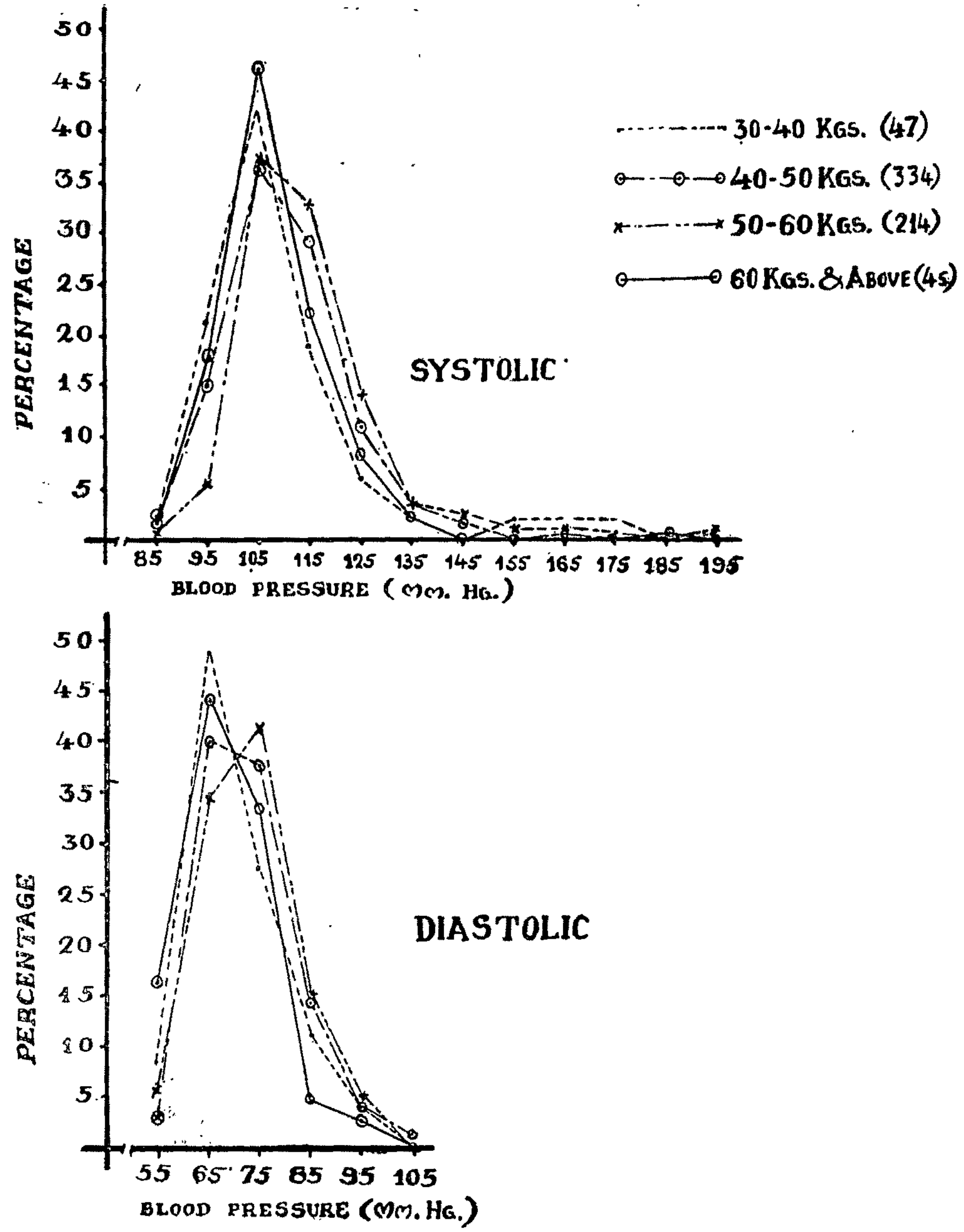
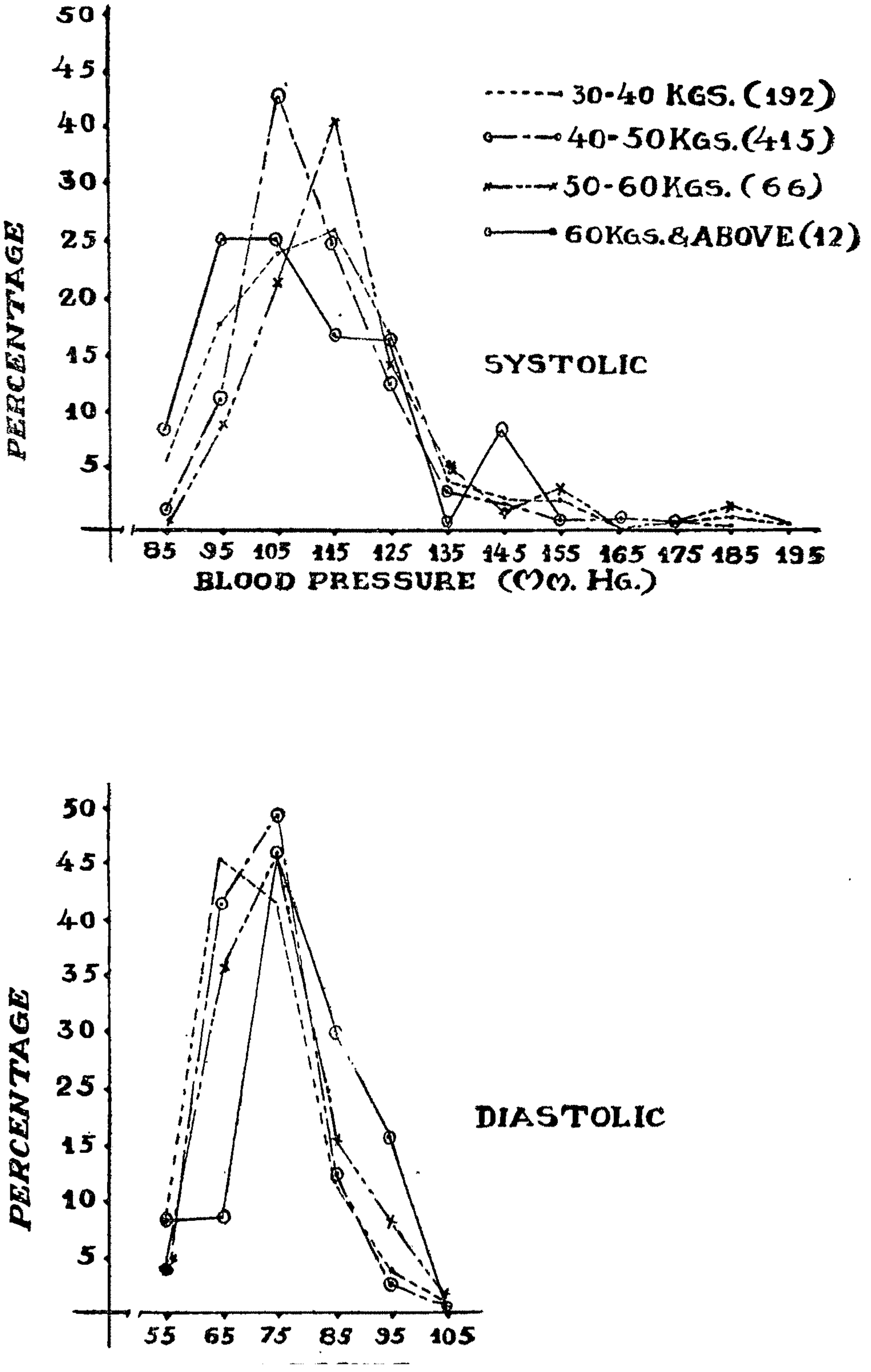


Fig. 1

Graph showing percentage distribution of systolic and diastolic blood pressure in females



Graph showing percentiles of systolic and diastolic blood pressure for males

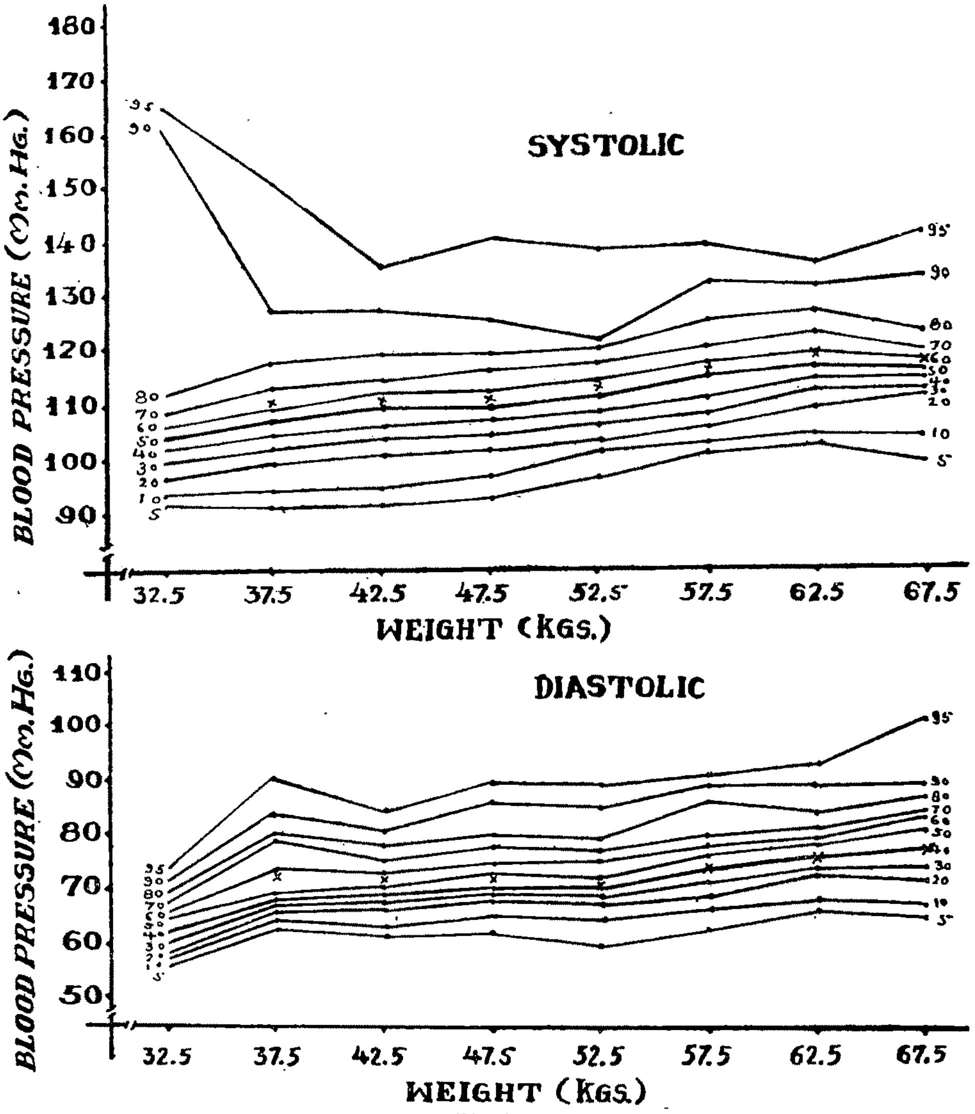


Fig 3

Graph showing percentiles of systolic and diastolic blood pressure for females

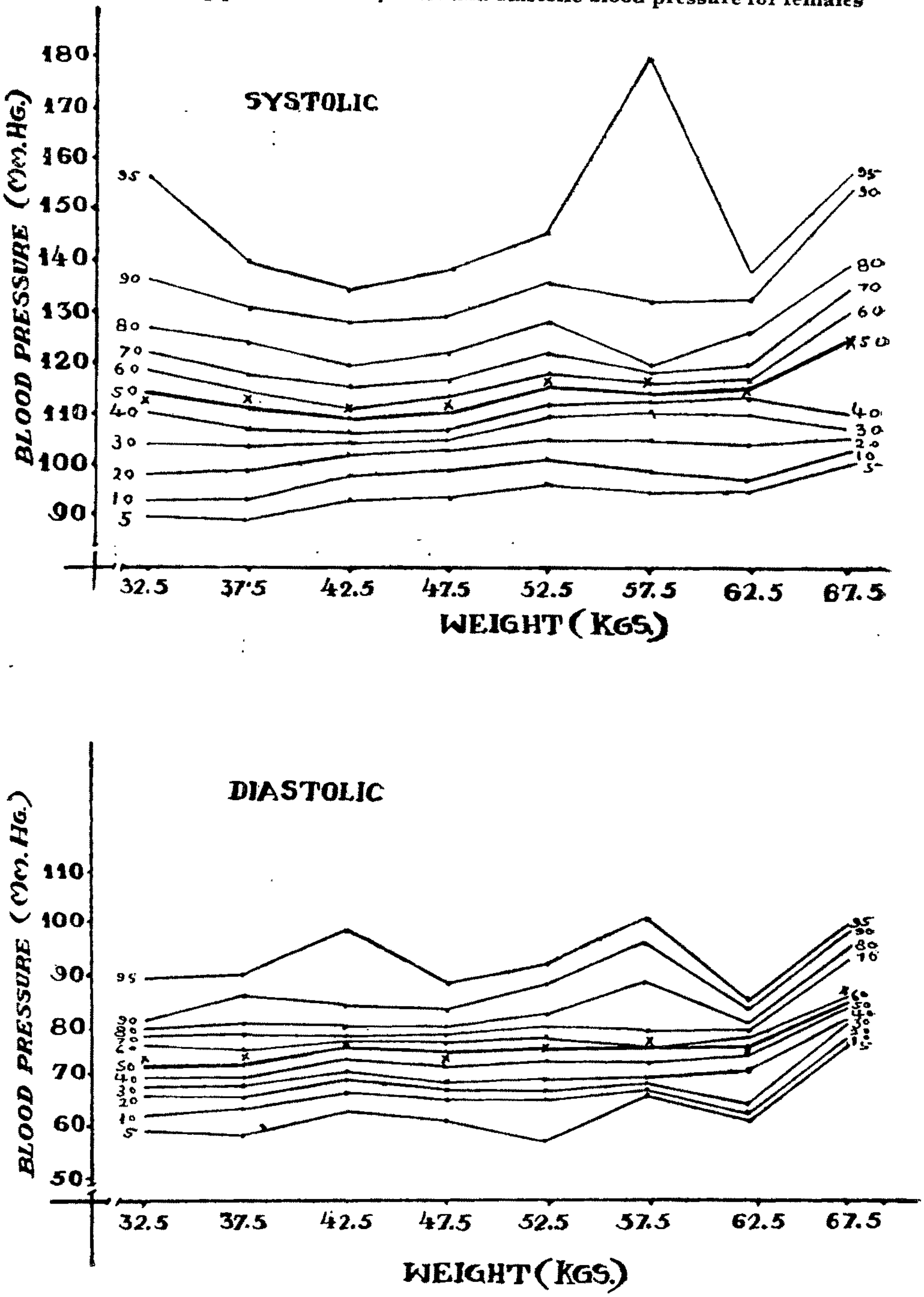


Fig. 4

Table I. **Showing mean and standard deviation of systolic and diastolic blood pressure by body-weight for both males and females.**

Body-Weight Kgs.	MALE			FEMALE		
	Frequency	Systolic	Diastolic	Frequency	Systolic	Diastolic
		Mean±S.D.	Mean±S.D.		Mean±S.D.	Mean±S.D.
30—35	9	109.40±20.40	64.60±5.10	46	112.80±15.03	72.61±9.15
35—40	38	110.26±16.50	73.04±8.75	146	111.85±15.90	73.22±9.35
40—45	124	110.33±12.90	72.17±8.75	267	110.77±12.60	73.50±8.20
45—50	210	110.57±12.60	74.12±8.80	148	112.44±12.80	73.85±8.15
50—55	152	113.09±12.00	73.00±8.45	48	117.10±13.90	75.10±9.50
55—60	62	116.13±15.00	76.21±8.60	18	116.67±18.90	76.40±10.85
60—65	28	117.50± 9.30	78.04±7.70	7	115.00±11.10	71.80±9.00
65 and over	17	117.35±10.00	79.56±9.55	5	125.00±18.90	86.50±7.30

Table II. Showing percentiles of systolic blood pressure for males by weight.

Percentiles	BODY - WEIGHT (KGS.)							
	30—35	35—40	40—45	45—50	50—55	55—60	60—65	65+
5.0th	91.5	91.3	91.2	92.7	96.0	100.8	102.3	98.5
10.0th	93.0	94.0	94.4	95.6	100.5	102.3	104.3	103.5
20.0th	96.0	98.7	100.4	101.0	103.1	104.9	109.3	110.4
30.0th	99.0	102.2	103.3	103.6	105.6	107.7	112.3	112.1
40.0th	101.5	104.5	105.4	106.2	108.1	110.4	114.4	113.8
50.0th	103.8	106.8	109.0	108.9	110.8	114.5	117.2	115.5
60.0th	106.0	109.2	112.3	112.0	113.8	116.6	119.0	117.2
70.0th	108.5	113.2	114.3	115.5	116.9	119.7	123.2	118.9
80.0th	112.0	118.0	118.7	119.0	119.9	125.0	126.7	123.0
90.0th	161.0	127.3	126.9	125.8	121.2	132.2	130.6	133.0
95.0th	165.6	151.0	135.6	129.8	138.0	139.8	135.3	141.5

Table III. Showing percentiles of diastolic blood pressure for males by weight.

Percentiles	BODY-WEIGHT (KGS)							
	30—35	35—40	40—45	45—50	50—55	55—60	60—65	65+
5.0th	55.8	64.5	60.4	61.5	58.7	61.8	65.8	64.3
10.0th	56.5	65.5	62.4	65.0	64.3	65.5	68.0	66.7
20.0th	58.0	66.5	65.5	66.7	66.4	68.1	71.6	70.6
30.0th	59.5	67.8	67.0	68.4	67.8	70.9	74.4	73.5
40.0th	61.5	68.9	68.4	70.3	69.3	73.9	76.1	77.0
50.0th	63.8	70.0	69.9	73.1	72.0	76.2	77.5	80.6
60.0th	65.6	73.8	72.6	75.1	75.0	78.0	78.9	82.7
70.0th	67.2	78.8	75.4	78.1	77.2	79.8	80.8	83.6
80.0th	68.6	79.6	78.3	80.2	79.1	85.5	84.3	87.0
90.0th	70.5	84.0	80.2	85.8	85.4	88.7	88.6	89.1
95.0th	72.8	90.5	83.6	90.1	88.8	91.1	93.0	100.8

Table IV. Showing percentiles of systolic blood pressure for females by weight.

Percentiles	BODY—WEIGHT (KGS.)							
	30—35	35—40	40—45	45—50	50—55	55—60	60—65	65+
5.0th	90.3	89.1	93.1	93.6	96.0	94.5	93.5	101.2
10.0th	93.1	92.6	97.9	98.5	100.7	99.0	97.0	102.5
20.0th	98.4	98.5	101.6	102.8	105.0	105.3	104.0	105.0
30.0th	104.2	103.6	103.8	104.7	109.4	110.4	110.3	107.5
40.0th	110.1	107.7	106.1	107.3	112.6	112.2	112.7	110.0
50.0th	114.2	110.6	108.3	109.8	115.3	114.0	115.0	125.0
60.0th	118.2	114.3	110.9	113.6	118.1	115.8	117.3	130.0
70.0th	122.3	118.2	115.1	117.5	122.0	117.6	119.7	135.0
80.0th	126.7	123.5	119.0	122.4	128.0	119.4	126.0	140.0
90.0th	136.0	130.5	126.7	129.1	136.4	132.0	133.0	155.0
95.0th	156.0	139.6	134.0	138.0	146.0	181.0	137.0	157.5

Table V. Showing percentiles of diastolic blood pressure for females by weight.

Percentiles	BODY—WEIGHT (KGS.)							
	30—35	35—40	40—45	45—50	50—55	55—60	60—65	65+
5.0th	58.8	58.5	61.4	60.9	57.0	65.6	55.9	76.1
10.0th	61.6	62.8	65.1	65.1	65.3	66.3	56.7	77.5
20.0th	65.4	66.1	67.8	66.7	67.3	67.6	58.5	80.0
30.0th	67.1	67.6	68.3	68.4	69.3	68.8	70.5	81.2
40.0th	68.7	69.4	69.9	70.4	73.2	70.2	74.0	82.5
50.0th	71.7	71.5	73.0	75.1	75.1	72.5	75 8	83.7
60.0th	75.8	75.4	75.6	76.5	77.4	74.8	77.0	85.0
70.0th	77.2	77.5	77.4	78.0	78.9	79.0	78.2	92.5
80.0th	78.6	79.5	79.1	79.4	82.3	88.5	79.3	95.0
90.0th	81.0	85.7	83.8	83.0	88.2	96.0	81.5	97.5
95.0th	88.5	89.9	98.4	88.3	91.5	100.5	83.5	98.8

for both pressures in each case. In case of systolic blood pressure for males, higher percentiles viz. 90th and 95th did not witness any evidence of increase with weight, while such percentiles for diastolic blood pressure of males and for both pressures of females showed considerable fluctuations. However, a tendency of both pressures, systolic as well as diastolic, to increase with weight for both males and females was observed.

Table VI, too, revealed that both blood pressure levels, systolic as well as diastolic in both the sexes were significantly positively related with weight, indicating a definite increase, on average, in the blood pressure levels with increase in body-weight. However, no significant difference in the degrees of relationship of both systolic ($Z= 1.4668$, $P>0.05$) and diastolic ($Z= 1.3892$, $P>0.05$) blood pressure levels in the two sexes was observed.

Quantification of average blood pressure levels in terms of weight was worked-out by evolving linear mathematical equations by the method of least square. Regression indicated (Table VII) that individuals, whose weight differed by, say 10 kg., their systolic and diastolic levels were expected, on average, to differ by 2.702 mm. Hg and 2.369 mm. Hg respectively for males and 1.517 mm. Hg and 1.619 mm. Hg respectively for females. This rise in blood pressure levels for both the sexes per unit increase in weight was found to be statistically significant.

Discussion

Blood pressure levels, found in the present study were lower than other clinic or hospital-based blood pressure studies (Gordon 1964 ; Acheson 1973). Since blood pressure measurements taken at clinics or hospitals tend to be higher than measurements taken at their homes (Ayman and Goldshine 1940) and thus, these lower levels might be due to the fact that readings, in the present context, have been taken at the innate settings of the respondents. Blood pressure levels, systolic as well as diastolic in the present study, were also observed to be considerably lower than that of blood pressure levels of urban adults of Allahabad Community (Indrayan **et al** 1972b) which might be indicative of relatively lower pressures in Indian rural adults than urbanities.

The observations revealed a significantly positive effect of body-weight on blood pressure distribution in the population studied but the pattern of influence in both the sexes was not uniform. For instance, shifting of distribution in case of systolic blood pressure to the right with minor changes in the degrees of dispersion, skewness and peakedness for each weight-group, was observed in males,

Table VI. Showing significance of correlation coefficients of systolic and diastolic blood pressure levels with body-weight for both the sexes separately.

Blood pressure levels	MALE			FEMALE		
	Correlation coefficient	t—value	P—value	Correlation coefficient	t—value	P—value
Systolic	0.1604	4.0856	<0.001	0.0807	2.1146	<0.05
Diastolic	0.1891	4.7927	<0.001	0.1142	2.9867	<0.01

Table VII. Showing significance of linear regression of systolic and diastolic blood-pressure levels on body-weight for both the sexes separately.

Blood-pressure levels	MALE				FEMALE			
	Constant	Regression coefficient	t—value	P—value	Constant	Regression coefficient	t—value	P—value
Systolic	98.31	0.2702	7.7487	<0.0001	105.46	0.1517	4.2203	<0.001
Diastolic	62.10	0.2369	4.6079	<0.001	68.80	0.1619	3.3633	<0.001

but in females, a distinct tendency of shifting of the distribution to the right for early weight-groups was seen and dispersion, skewness and kurtosis also increased considerably. Similarly for diastolic, such characteristics were also slightly different in both the sexes. However, the extent of relationship of both systolic and diastolic pressures with body-weight did not show any significant difference ($P>0.05$) in the two sexes.

Percentile-analysis of both pressures, systolic as well as diastolic for both males and females also showed a tendency of rise in blood pressure levels with increase in body-weight. Such significant ($P<0.001$) rise in the blood pressure levels per unit increase in weight, as evidenced by regression-analysis of blood pressure on weight, also clearly suggested a definite increase in the quantum of both the pressures with advancing weight in the two sexes. The unexpected finding of the percentile-analysis, relating to the higher percentiles of systolic blood pressure **viz.** 90th and 95th percentiles in case of males and 95th percentile in case of females, which did not witness any evidence of rise in the quantum of blood pressure levels with weight, does not necessarily indicate that such a case has ever taken place in any of the individual studied, however, this could be the case. The mathematical fit (Table VII), expressed in the form of linear regression equations of blood pressure levels on weight, also enables, to a considerable extent, to predict the expected value of systolic and diastolic blood pressure levels in terms of weight for both the sexes.

Florey and Acheson (1959), when discussing the influence of eight variables including weight on blood pressure levels for United States men and women, have presented significantly positive correlations of systolic as well as diastolic levels of blood pressure with weight. Evidences of advancement in blood pressure levels per unit increase in body-weight have also been witnessed by Kannel **et al** (1967), Miall **et al** (1968), Harlan **et al** (1962) and Fetcher (1954). The results of the present study resembled with those discussed by Florey and Acheson (1969), Kannel **et al** (1967), Harlan **et al** (1962) and Fetcher (1954) **etc**, witnessing significant positive correlations of systolic and diastolic levels of blood pressure with body-weight.

The present blood-pressure analysis is a population based, cross-sectional study and as such has certain limitations common to such sort of studies. Also, the present analysis excludes the effect of some significant correlates of blood pressure **viz.** age and body-built **etc.** which are known correlates of weight also. Thus, the actual extent of relationship of blood pressure levels with body-weight, after eliminating the effect of these correlative factor from both, blood pressure and weight, might be lower than those presented here. However, the relationship of these two parameters needs further investigation.

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Study of Human Skin for Determination of Age at Pre-natal Life

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Received for publication, November 30, 1976.

The skin of palm and sole were studied at different ages at 30-200mm C.R. length in the prenatal life with special reference to the sweat glands and stratum granulosum.

Introduction

Few authors have studied the skin in general and palm and sole in particular in relation to their changes at pre-natal life. Hamilton et al (1972), Harrison (1963) and Keith (1948) have stated that epidermis is formed by cuboidal cells. The periderm consisting of flat cells forms the protective layer. Arey (1961) has mentioned that the periderm is formed in the fifth week of intrauterine life whereas epidermis has three layers by the third and fourth month of embryonic life. After the fourth month the epidermis is highly stratified. He has also stated that the stratum granulosum contains, Kerato-Hyalin granules and this by fusion forms alidine. Palherkar (1965) studied the microscopical changes due to age in the foetal skin during 5 to 9 months. Pattern (1968) has stated that the deep lying layer of cells become sharply distinct from the rest of the epithelium, which constitutes stratum germinativum, the cells of which show a dense, strongly staining cytoplasm and well marked cell boundaries. Longman (1975) has stated that at the end of fourth month the epithelial layers constituting the epiderms of the skin acquire thin, definitive arrangement and four layers can then be distinguished.

The object of the present work is to study the layers of skin of palm and sole of foetus between the age of 3 to 6 months of prenatal life with special reference to stratum granulosum and sweat glands, as this is the distinguishable layer than the general body surface.

Meterial and Methods

Thirty human foetuses of either sex of different length from 30 to 200 mm C.R. length were studied. The skin of palm and sole were fixed in 5 per cent formal saline. The sections were cut at 6μ thickness. Haematoxyline, Permanganate and

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*Professor of Anatomy and Principal

Congored were used. H. E. stain were used to study different layers whereas H and P congored were used to study stratum granulosum, to study the Keratohyalin and alidine. The section cutting of the skin at the early age is quite difficult as the epidermis and dermis separate very easily during sectioning.

Observation

Palm and sole with 43 and 53mm C.R. length show well formed, stratum Basalis and pariderms (Plate III, Fig. 1). At 64mm stage the intermediate layer is also developed. At 70-80mm stage there is not much of difference in the palm and sole. Solid bud like down-growths at regular intervals imparting wavy appearance of the basal layer appeared at 97mm stage. The average number of down-growths is about 25 to 30 in a length of one mm. In the sole these down-growths are not as many as seen in the palm but the section appears more vascular than the palm. The 103mm stage shows the formation of sweat glands by further down-growth of the buds from the basal layer (Plate III Fig. 2). By 115 mm stage the down-growths are channelised to form the sweat glands ducts. The secreting parts of the glands are deeply situated in the dermis. The 120mm stage also show the same appearance. At 135mm length, palm and sole show continuous one cell thicker layer of spindle shaped cells which contain granules (Plate IV, Fig. 3). These granules are stained deeply with haematoxyline and Permanganate as they contain Keratohyalin. By 140mm stage subsequently the stratum corneum develops.

Discussion

By the study of sections of palm and sole at different ages show that it is difficult to differentiate the palm and sole upto 80mm C.R. length but the stratum basalis presents a straight layer. After this stage changes occur to form down growths (Papillae) more in number in the palm than in the sole. The stratum granulosum one cell thick layer appears at 135mm C.R. length. The exact time of appearance of the stratum granulosum has not mentioned earlier. The above study in development of sweat glands and stratum granulosum in the skin of palm and sole of foetus is an additional factor for the determination of viability of foetus.

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PLATE III

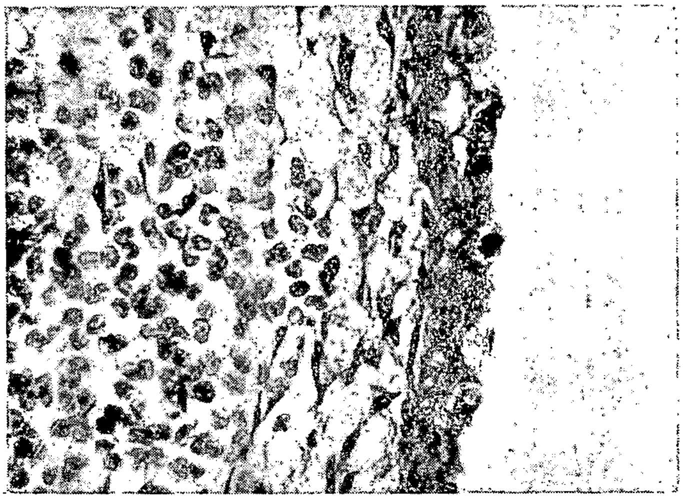

Fig. 1. Photomicrograph showing well formed stratum basale and epidermal cells. The dermis is quite vascular x 600 HE

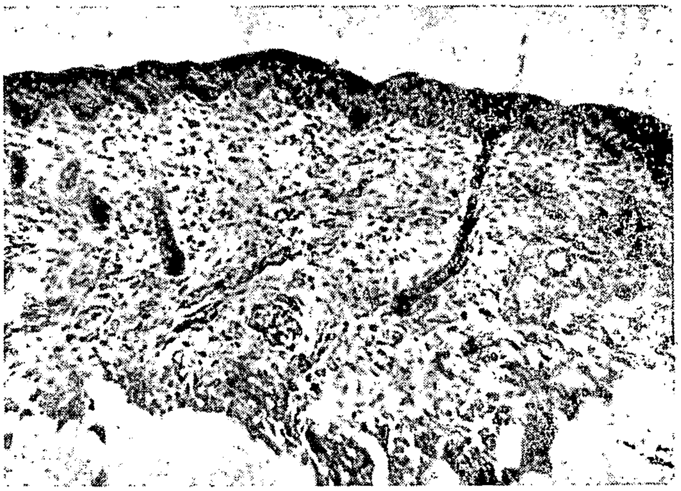

Fig. 2. Photomicrograph showing downgrowth of buds from basal layer are noticed and one bud showing channelised sweat gland. x 400 HE

PLATE IV

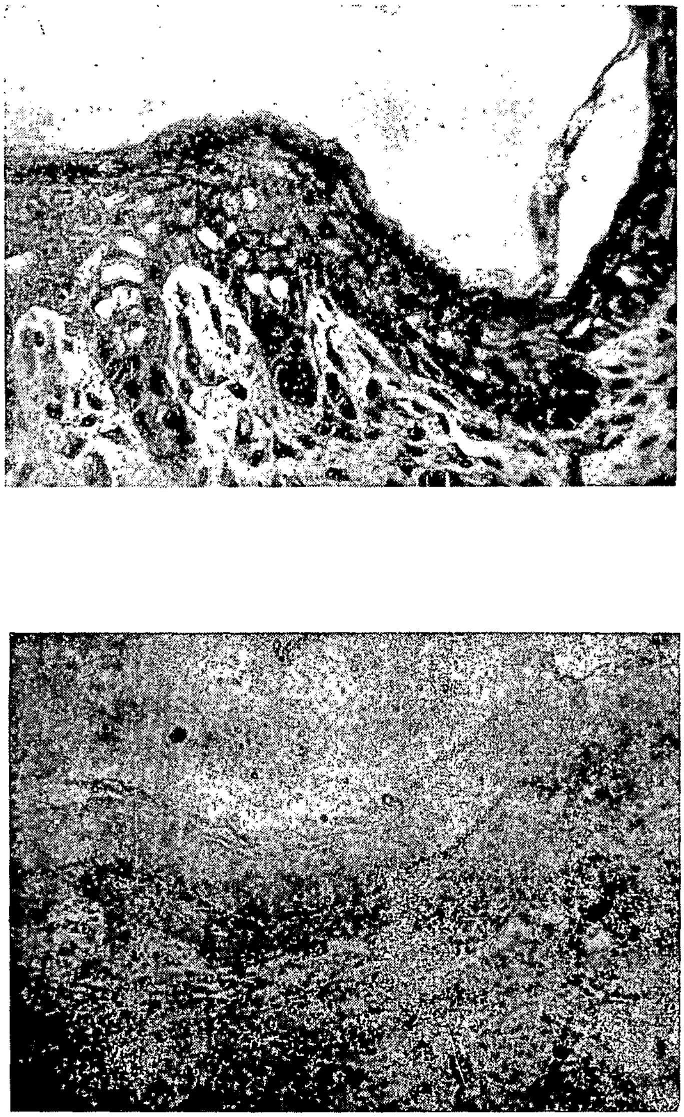

Fig. 3. Photomicrographs showing continuous cell layer of stratum granulosum in low power which in high power shows spindle shaped cells with granules x 400 HE and x600 HE

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Abstracts

Abstracts of the papers read at the 14th meeting of the North Chapter of the National Academy of Medical Sciences held at Medical College, Amritsar on Sunday the 27th March, 1977.

Immunoglobulins and Complement Levels in Invasive Amoebiasis

R. C. Mahajan, N. K. Ganguly, S. Sharma, D. V. Datta and P. N. Chhuttani

Departments of Microbiology and Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh.

Immunoglobulins (IgG, IgA and IgM) C'3 and CH_{50} levels have been estimated in 43 cases of amoebic liver abscess, 13 cases of intestinal amoebiasis and 28 normal healthy controls. IgG, C'3 and CH_{50} were found to be significantly high in amoebic liver abscess cases than in other groups. Not much change was noticed in IgA and IgM levels. Considerable overlap in different parameters was noticed with liver abscess group. Th· role of these parameters for prognostic value in amoebiasis is discussed.

Arsenicosis—A new disease

D. V. Datta, M. K. Kaul and Iqbal Singh

Department of Hepatology, Postgraduate Institute of Medical Education and Research, Chandigarh

Arsenic is prescribed freely in India by ayurvedic and homeopathic practitioners. Recently presence of high arsenic concentration in some of springs and wells has been reported by our team (Datta and Kaul 1976). The finding of high liver arsenic in some patients of idiopathic portal hypertension has created a great interest and this condition is termed as arsenicosis (Datta, 1976). The present study reports detection of high concentration arsenic in opium samples sold illegally. It was found to be present in free form. The precise source of arsenic in opium cannot be stated with certainty. It is found that arsenic (Sankhya) is used as an additional aphrodiase by the illegal sellers which may explain the variable levels of arsenic in opium samples obtained by us. Field surveys which are in progress has revealed hepatomegaly, peripheral neuritis and skin pigmentation in some of the patients consuming adulterated opium. The scope of these findings will be discussed.

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Design of Splints and Study of their Effectiveness in Preventing Skin Graft Contraction in Management of Post-burn Deformities

C. P. Sawhney

Department of Plastic Surgery, Postgraduate Institute of Medical Education and Research, Chandigarh

Development of a contracture following skin grafting of deep burns and recurrence of contractures after treatment is common if not invariable and is due to contraction of skin grafts. Measures to counteract this have so far been half hearted and limited to few regions of the body **e.g.** neck. The author, over the years, has designed simple and cheap splints which can be easily fabricated from materials available locally, which are worn following operations. The designs vary from region to region depending upon anatomical variations and local requirements. The paper deals with design of splints, their rationale and their effectiveness. It also presents the results achieved following their use even in some of the gross post-burn deformities which are sometimes considered intractible.

Sodium Nitroprusside as Hypotensive Agent in Neurosurgery

Y. S. Varma

Department of Anaesthesiology, Medical College, Jammu

The use of sodium nitroprusside as a safe, cheap, convenient and easily available hypotensive agent is discussed and its more generous use is recommended in neurosurgery. The drug only very rarely fails to produce hypotensive, or suffers from tachyphylaxis. There is no cross tolerance with Arfonad (Trimetaphan). It maintains the brain blood flow even under hypotension and yet does not appreciably increase the brain bulk or intracranial tension. By causing cerebral vasodilation, a lower level or systemic blood pressure is better tolerated than with other hypotensive agents. Post-operative brain damage due to hypotension was not noted even in cases where profound hypotension ("Dip") was used for periods upto 5-6 minutes. No retractor anaemia was seen. Due to evanescent action of drug the time of "Dip" was easily controllable. Recovery of patients was satisfactory without appreciable harmful effects. No reactionary hemorrhage was seen.

Pattern of INA Synthesis in Nutritional Vs. Neoplastic Megaloblastosis

K. C. Das and G. Garewal

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Nutritional megaloblastosis (**i.e.** megaloblastosis due to deficiency of folate and/or vitamin B 12) is characterised by an abnormality of DNA synthesis in bone marrow cells and PHA stimulated lymphocytes. In these cell systems it has been demonstrated that the **in vitro** incorporation of H^3 thymidine (H^3TdR) into DNA cannot be suppressed by excess of nonradioactive deoxyuridine in deficiency of one or either of these vitamins. This finding has been utilised for the development of a biochemical test (deoxyuridine suppression test) to define megaloblastosis as well as the kind of deficiency causing it.

Megaloblastic erythropoiesis occurs not infrequently in the bone marrow of patients with erythroleukaemia and acute myeloblastic leukaemia. The precise biochemical mechanism of such changes remain obscure. The present communication describes the results of studies of DNA synthesis in bone marrow of patients with these haemopoietic neoplasia. It was observed that the deoxyuridine suppression test (deoxyuridine suppression of H^3-TdR incorporation into DNA) remains normal in **in vitro** studies of bone marrow of these patients. Furthermore, autoradiographic studies and liquid scintillation counting for the incorporation of thymidine into DNA by bone marrow cells reveal significantly reduced DNA synthesis as compared to normal marrow cells. It is postulated on the basis of these findings that the molecular basis of defective DNA synthesis in neoplastic megaloblastosis consists in metabolic defects mediated by the apoenzymes rather than the co-enzymes.

Compression of Common Peroneal Nerve : Occupational Hazard Among Farm Workers

Hardas Singh Sandhu

Department of Orthopaedics, Medical College, Amritsar

During the period 1965-76, 33 cases of paralysis of the common peroneal nerve were seen among farm workers. All the patients were 18-28 years of age. Paralysis had appeared after a person had been working in a sitting position with forward bending—a posture commonly adopted for harvesting a crop or hoeing. The symptoms were of 3 days to 3 years duration. There was a sensory impairment and motor deficit in the distribution of the common peroneal nerve particularly affecting the muscles of anterior compartment. Exploration of the nerve was carried out in 15 cases, and it was found to be compressed by a tendinous arch extending along the posterior border of the proximal part of the peroneus longus and then curving backwards and upward along the lateral border of the soleus muscle. Excision of this tendinous arch and elimination of origin of peroneus longus from the neck of the fibula lead to improvement in the neurological deficit.

A study of the incidence of this tendinous arch in the normal population carried out on cadavers and persons undergoing operations in this region for causes other than common peroneal nerve lesions, revealed that it was present only in 5 out of 85 instances.

Our Experience with Rhinoplasty (Combined Technique Rhinoplasty)

Yoginder N. Mehra and G. S. Dwivedi

Department of Otolaryngology, Postgraduate Institute of Medical Education and Research, Chandigarh

The senior author has done corrective rhinoplasties since 1963 using Joseph's subcutaneous intranasal technique. Lateral and median osteotomy was done by sawing (difficult procedure). The resultant bone dust also lead to some broadening of the nasal bridge. There was also nasal obstruction in a few cases.

Having observed these difficulties, a combined technique rhinoplasty was undertaken since 1973. In this technique the lateral superior and median osteotomy are performed with an osteotome after small incision on the skin.

The results of this technique (21 patients) have been compared with Joseph's technique (11 patients). Where combined technique was used, broadening of the nasal bridge was not seen and no cases showed postoperative nasal obstruction. It is an easier procedure and usually takes half the time as compared to the intranasal technique (Joseph).

Dilantin-induced Megaloblastosis : A Biochemical Study

K. C. Das

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A qualitative biochemical lesion in nutritional megaloblastic bone marrow and lymphocytes, is characterised by defective de novo synthesis of thymine-DNA, as demonstrated by the failure of exogenous deoxyuridine (dU) to suppress the incorporation of radio-active thymidine (^{33}H-TdR or ^{125}I-UdR) into DNA (abnormal dU suppression). This abnormality can be corrected **in vitro** DNA-synthesis by bone marrow cells and PHA-stimulated lymphocytes in 5 patients with dilantin-induced megaloblastic anaemia. It was observed that the incorporation of ^{3}H-TdR into DNA in both cell system was significantly impaired in the presence of dilantin and the "dU suppression abnormality" was much less pronounced in dilantin-induced megaloblastic marrow and lymphocytes. These findings suggest that dilantin impairs DNA-synthesis possibly by acting on the apoenzymes rather than the coenzymes of the DNA-synthetic pathways and may account at least in part for the development of megaloblastosis.

Metabolism of Antipyrine in Patients with Liver Disease

A. P. S. Narang and D. V. Datta

Antipyrine has been used as a model drug to investigate the effects of liver disease on drug metabolism in man. The study was carried out on 22 patients with liver disease and five healthy controls. A single dose of antipyrine (10mg/kg.) was given by intravenous infection. A prolongation in antipyrine half-life ($T\frac{1}{2}$) was found in patients with liver disease, patients with viral hepatitis showed a greater increase in $T\frac{1}{2}$ than in others. There was a significant increase in $T\frac{1}{2}$ of patients with intra-hepatic portal hypertension in which liver function tests are shown to be normal, suggesting that the cause of these changes was due to defective drug metabolising enzyme system.

Role of Urethral Organisms in the Causation of Lower Urinary Tract Infection

Sotantar Rai

Department of Surgery, Medical College, Amritsar

The present study was undertaken to find out the role of urethral meatus organism if any in the causation of lower urinary infection after tying in an indwelling catheter. Fifty males having retention urine due to benign hypertrophy of the prostate were the subjects. Urethral swabs from the fossa navicularis and the urine culture specimens were taken at the time of admission and on the 4th and 7th catheterise day. Urethral swabs and urine culture studies were done. The data was subjected to analysis and it was found that despite rigid asepsis and closed drainage an indwelling catheter raises the risk of the uretheritis and cystitis. In as high as 70 per cent of the cases infection is believed to have travelled from the meatus to the urinary bladder after tying in the catheter.

Trace Metal Pattern in Patients of Myocardial Infraction and Hypertension

R. Nath, A. Achamma* and B. Cowan*

Department of Biochemistry, Postgraduate Institute of Medical Education and Research, Chandigarh

Relationship between trace metals and cardiovascular disease has been recently implicated by a survey of WHO/IAEA (Technical Bulletin No. 520, R. Massaroni, 1974). The present study has been carried out in fifty patients of myocardial infraction and hypertension and in twenty five control subjects. Effect of various factors like (a) geographical location i.e. rural and urban (b) diet i.e. vegetarian and non-vegetarian, has also been assessed on tracemetal pattern. Copper, zinc, calcium and magnesium have been measured in both plasma and urine by Atomic Absorption Spectrophotometer. The data has been statistically evaluated by t-test.

Significant increase in plasma zinc/copper ratio ($p<0.05$) and increased urinary excretion of calcium and zinc ($p<0.02$ and <0.001 respectively) has been observed as compared to normals. In patients of hypertension, however, increased urinary excretion of magnesium and zinc ($p<0.05$ and <0.001 respectively) has been noted. Alteration in calcium and magnesium concentration were observed in the urban group, while rural group showed significant alteration in copper and zinc. Vegetarian group showed significant alteration in copper and zinc concentration both in plasma and urine as compared to non-vegetarian group. The data indicates that the tracemetals are significantly altered in hypertension and myocardial infraction.

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*Department of Medicine, Christian Medical College, Ludhiana.

Cellular Versus Humoral Immunity in Experimental Plasmodium Berghei Infection

Aruna Parashar, B.K. Aikat, S. Sehgal and S. Naik

Department of Pathology, Post Graduate Institute of Medical Education and Research, Chandigarh

Experimental induction of malaria was carried out in Swiss inbred strain of mice. Chronicity was maintained by repeated passage of 10^3 parasitized R.B.Cs. and subsequent therapy with antimalarial drug. Transferred immune sera, lymphoid cells of thymus, lymphnode, spleen and peritoneal macrophages in age and sex matched recipients. Control group received normal cells from animals and subsequently challanged with standard dose of parasite.

(i) It was observed that immune sera in high doses resulted in enhancement of parasitaemia however when used in lesser amounts it afforded protection.

(ii) Viable immune lymphocytes of thymus and lymphnode afforded protection and also the mixed population of spleen and peritoneal exudate protected the animals against challenge inoculum.

(iii) Also the glutaraldehyde treated spleen cells and material obtained after freeze thawing of same number of cells from spleen, macrophages and lymphnode also protected the animals.

These findings show that under the experimental conditions immunity against **P. berghei** infection is mediated through (i) specific antibody which is dose dependent ; (ii) CMI ; (iii) effective response to processed antigen.

Hepatic Veno-occlusive Disease caused by Helitropium

D.V. Datta, M.S. Khuroo, P.N. Rao and B.K. Aikat

Division of Hepatology, Postgraduate Institute of Medical Education and Research, Chandigarh.

Two patients of hepatic venu-occlusive disease are recorded caused by consumption of toxic helitropium plant, **Hathi-sund**. The plant was used as a medicinal herb for treating grand mal epilepsy. A unique opportunity to study the course of illness of these patients was present while they were on long term treatment with hepatic microsomal enzyme inducers phenobarbitone and phenytoin sodium. The severity of illness inducing hepatic encephalopathy, gastro-intestinal bleed, and deep jaundice is related to their prior drug therapy.

Ann Natl Acad Med Sci (India), 13, 3, July—September 1977

Letter to the Editor

Dear Sir,

I am happy to go through your editorial—New **Horizons in Health Care**—published in the Oct.-Dec. 1976 issue of the ANNALS. It is heartening to note that the country is thinking to deviate from the old orthodox system of health cover to the masses by way of new community level health workers scheme.

In the community level health workers scheme as you have rightly pointed out there can be some amount of quackery by escalations of this programme especially the abuse of drugs which is already on high side. As you have pointed out in the first paragraph the education of older generation by way of mass media communication may not achieve its full objective because of the orthodox ideas of the adult population.

As a member of the Academy I would like to opine that we should adopt a policy of 'Prevention is better than cure' by which the task of the Government in the field of public health will be much reduced. This prevention of diseases can be mainly achieved by educating the masses especially the younger generation but not necessarily the older generation. Thus it will be more proper to educate the younger generation by way of school teaching. This can be achieved only by inclusion of subjects like Medical Science, Public Health, primary chapters of Pharmacology, Surgery etc. in the school syllabus. In the field of Veterinary Science also it will be highly essential to include such subjects as Veterinary Medicine and Animal Husbandry in the curriculum of the primary as well as Higher Secondary School syllabus in order to educate the younger generation the importance of animal disease, its prevention and the zoonotic importance. Thus the syllabus of the schools can be revised to include certain primary lessons of medicine, public health, surgery and veterinary medicine, with the motto that every citizen should primarily be a public health officer rather than a doctor.

At present the subjects like Botany and Zoology which have got less relevance in the day to day living of an ordinary citizen can be replaced by more relevant subjects mentioned above. This will enable to develop a new generation having more sense about the public health, hygiene in public places, necessity to prevent various diseases by way of inoculation including the animal diseases. Such measures only can help to improve the health of the village population lessening the burden on the Government to extend the health cover through various ramifications to reach the village farmers.

Hope you be able to appreciate the contents of this letter and if neecssary may place the same before the Academy for a detailed discussion of the pros and cons of including the public health and veterinary medicine subjects in the school syllabus.

Yours sincerely,

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Ann Natl Acad Med Sci (India), 13, 3, July-September 1977

NATIONAL BOARD OF EXAMINATIONS

Membership of the Academy of Medical Sciences, February, 1978
(Qualification included in First Schedule MCI ACI, 1956)

Application for the next examination to be held in February, 1978 will be received till 31st October, 1977 in the following specialities. Only Medical graduates are eligible to apply.

1. **Division of Basic Medical Sciences:** Anatomy, Physiology, Pathology, Microbiology and Pharmacology.
2. **Division of Medicine and Allied Seicnces:** General Medicine, Pediatrics, Psychiatry, Dermatology, Radio-diagnosis and Radio-therapy.
3. **Division of Surgery and Allied Sciences:** General Surgery, Orthopaedic Surgery, Ophthalmology, Anaesthesiology, Obstetrics & Gynaecology and Otorhinolaryngology.
4. **Division of Community Health:** Social & Preventive Medicine, Integrated Maternal Child Health Care, Health Administration including Hospital Administration, Health Education, Epidemiology, Occupational Health and General Practice.

The written examination may be held at different regional centres which will be announced later.

Full particulars and application form can be had from the Secretary, National Board of Examinations, C-II/16, Ansari Nagar, Delhi-110016. on request indicating the particular subject in the division concerned latest by 7th October, 1977.

Ann Natl Acad Med Sci (India), 13, 3, July—September 1977

NATIONAL ACADEMY OF MEDICAL SCIENCES (India)
C-II/16, Ansari Nagar, New Delhi-110016

Notice

The National Academy of Medical Sciences (India) will award the following medals or prizes during the year 1977-78.

1. Through the courtesy of Late Dr. S. S. Misra, a founder Fellow of the Academy, Dr. S. S. Misra Memorial Bronze Medal plus cash prize will be awarded for the best unpublished work in any field of bio-medicine by a young bio-medical scientist (below 40 years). Papers submitted by other scientists who are not considered worthy of Bronze Medal plus cash prize may be awarded certificates of merit by the Academy.

2. Through the courtesy of Shriram Foundation, the Academy will award Sir Shriram Bronze Medal plus cash prize to a bio-medical scientist for his/her best published paper during the preceding three years on all Basic Sciences subjects. The work should have been done in India by any bio-medical scientists of any age. The scrutiny of the joint paper will only be done if the first name of the joint paper is that of the candidate applying for the award.

3. Through the courtesy of Dr. R. M. Kasliwal, a Founder Fellow of the Academy, Dr. Kasliwal Prize/Medal will be awarded to the best worker in the field of ‘COLON AND ITS DISEASES’. No restriction of age. The nominee will have to supply alongwith his/her paper, complete bibliography on this subject including work done in India.

4. Through the courtesy of Dr. (Mrs.) Vimla Virmani, a senior Member of the Academy, Dr. Vimla Virmani Bronze Medal plus cash prize will be given to a Bio-Medical Scientist below the age of 45 years for his/her best work in the field of “Rehabilitation of the Neurologically Handicapped patients based on published or un-published work with particular emphasis on the applicability of the work of socio-cultural and economic considerations prevalent to the Indian Community/Communities”.

Conditions :

i. The scientist should not have received any prize for the same paper/s in the past ;

ii. Four copies of each paper should reach the Office of the Academy latest by 15th October, 1977. These should be accompanied by a forwarding letter giving a brief bio-data of the scientist along with the title of medal/prize for which the paper/nomination is submitted ;

iii. Selected papers for Dr. S. S. Misra Memorial Bronze Medal/Certificates of Merit and unpublished papers for Dr. Vimla Virmani Award will be published in the Annals of the National Academy of Medical Sciences ;

iv. Scientists selected for medal/prize or certificate of merit will be invited at the cost of the Academy to present their papers at the annual meeting of the Academy in January, 1978.

v. The awards will be formally presented at the time of the Convocation of the Academy on the next day of the presentation of the paper.

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The Annals of the National Academy of Medical Sciences, (India) appearing trimonthly welcomes well-organized original contribution on all topics in biomedical sciences. Manuscript should be typewritten carefully in double spacing on one side of the paper of uniform size and with sufficient margin. Two copies of the manuscript complete with figures and tables should be submitted to : The Editor, Annals of the National Academy of Medical Sciences, (India) C-II/16, Ansari Nagar, New Delhi-110016. Submission of a manuscript in this journal implies that it has not been published and is not under consideration for publication elsewhere.

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Introduction should be brief and state precisely the scope of the paper and the essential background necessitating investigation done.

Material and Methods should be described briefly and reference to the sources (e.g. Sanyal, 1970) should be given. New matters however, may be given in detail.

Results should be brief and only relevant data should be given. The data should be statiscally analysed, and the P value should be given.

Tables should be short and restricted in number. An illustration (photographs or line drawing) should be about 1½ times the reproducable size. Glossy prints of photographs are preferred . Any lettering or annotation on photographs or line drawings should be indicated on a tracing paper or a legend sheet. The name of the principal authour and the figure number should be written on the back of the illustrations.

Discussion should be logical and should be related to the significance to the work done.

References cited in the text should be listed in an alphabetic sequence. Citations should be presented in the reference list as follows :

Chakravarty, N., Goth, A. and Sen. P. 1973. Potentiation of dextran induced histamine release from rat mast cells by phosphatidyl serine. **Acta Physiol Scand 88,** 496.

Sen, P. and Sanyal, R. K. 1969. Experimental studies on antigenicity of penicillin. **In Aspects of Allergy and Applied Immunology 2** 123. Edited R. Viswanathan, R. K. Sanyal, G. Bazaz-Malik, S. Arora and B. D. Miglani, New Heights, Delhi.

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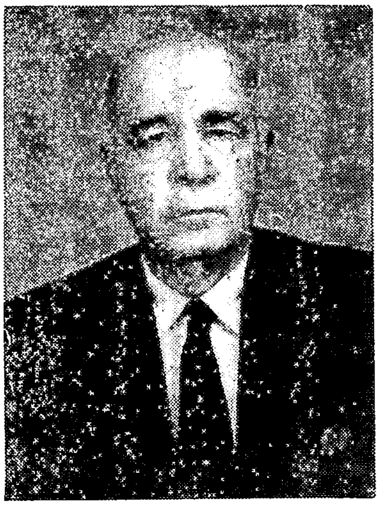
Obituary



LT. COL. SANGHAM LAL (25.9.1901—9.8.1977)

On 9th August, 1977, medical fraternity lost a zealous scientist and a surgeon of great national and international repute in Col. Sangham Lal who died in a car accident in U.K. under very tragic circumstances. Col. Sangham Lal was a man of outstanding personality and sterling character. He was truly dedicated to his work and made significant contribution to the field of General Surgery. He was an able administrator.

Col. Sangham Lal was born in Agra, U.P., on 25th September, 1901. He obtained his M.B.B.S. degree from Punjab University in 1924 topping the final MBBS examinations in the whole university and was awarded a Gold Medal. He did his F.R.C.S. (Eng.) in 1929 and passed D.O.M.S. (London) examination in July 1930.

His eminent service career started in 1926 when he joined the Indian Medical Service and later got his permanent Commission in 1931. He was transferred to the Civil IMS Madras Cadre in 1934. From 1934 to 1937 he was Civil Surgeon, Trichnapalli ; Prof. of Surgery, Madras Medical College, Madras from March 1937 to June 1938. During the Second World War (1939-45) he was Surgical specialist and O.C. Surgical Division with the rank of Lt. Col., 7 Indian Base General Hospital, Kirkee. On reversion to the Civil Madras Cadre, he became Prof. of Surgery and Superintendent of General Hospital, Madras, 1946-51 ; and Director of Medical Services, Madras, 1953-57. He made great improvements in Medical Education and Medical and Health Services and all specialities in the Tamil Nadu state. He was appointed the first Prof. of Surgery, A.I.I.M.S., New Delhi, in 1958 and held it till 1961 with great distinction.

Col. Sangham Lal was a founder fellow of the Academy and its Secretary and Executive Director right from its inception till March 1969. He had to steer the ship through many storms and overcome many obstacles and hurdles during its infancy with great tact, preservance and foresight. His devotion to the cause of the Academy and selfless services were responsible for its present stature. Rightly speaking he can be called one of the Chief architects of the National Academy of Medical Sciences (India). He introduced many changes in the Rules and Regulations, the last one for the election of the President by the General Body of all the Fellows. He was working hard for raising the ethical standards of the Academy and the Fellows.

Besides being a founder fellow of the Academy and a fellow of the Royal College of Surgeons, London, he was a member of the various specialist organisations. He was a Past President of Association of Surgeons of India ; Indian Society for Gastro-enterology ; Madras Dental Council ; and Madras Pharmacy Council. He was Member of Madras University Senate, Medical Council of India and Scientific Advisory Board, ICMR. He was Examiner for M.B. and M.S. examinations of most of the universities in India. He was the Editor of 'Text book of Surgery'. He visited U.S.A., U.K. (Rockfeller grant to observe advances in Education Science). As the Executive Director of the Academy he visited Canada in 1967 at the special invitation of Manitoba Foundation.

His death is a great loss to the medical profession and medical scientists and the National Academy of Medical Sciences (India). The country has lost a great medical administrator. He will long be remembered with gratitude, respect and affection by a large circle of friends and colleagues.

He is survived by his wife, two sons and a daughter.

K. N. RAO

Ann Natl Acad Med Sci (India), 13, 4, Oct.—Dec. 1977

Obituary

DR. J.G. PAREKH (1910—1977)

The academic and professional medical world deeply mourns the passing away of Dr. J. G. Parekh.

After securing the M.B.B.S. (Bom) in 1934 he took the L.R.C.P., M.R.C.S. (Eng.) in 1935 and the M.R C.P. (Lond) in 1936.

On his retrun to Bombay he started private practice as a Consulting Physician and Pathologist In 1938 he was appointed Honorary Assistant Physician to the J. J. Hospital and Tutor in Medicine at the Grant Medical College. For a short period during World War II he acted as Professor of Medicine at the Grant Medical College.

In 1956, he was appointed Head of the Medical Unit at the J. J. Hospital, a post he held till his retirement in 1968.

Though his teaching duties were essentially concerned with general medicine, his basic interest lay in Haematology, a subject to which he contributed almost a hundred papers of excellent quality.

He was elected President of the Haematological Society of India and President of the Association of Surgeons of India in 1969.

He was Fellow of the Asian and Pacific Society of Haematology, corresponding Member of the Swiss Haematological Society and a Member of the Expert Group of the Haematological Committee of the I.C.M.R. He was largely responsible for starting the "Haemophilia Association" which has received recognition from the World Federation of Haemophilia.

His deep knowledge of his specialised area of work and his powers of expression made him a popular chairman at lectures and symposia in conferences all over the country. His contribution to the Text Book of Medicine of the Association of Physicians of India was considerable and he edited the Section on Haematology in all 3 editions of the book.

He delivered the Dhayagude Memorial Oration on "Haemorrhagic Disorders" in 1965 and the Jagatram Vaidya lecture on "Recent trends in Haematology" in 1961.

He was an examiner in both undergraduate and post-graduate examinations all over the country. A popular teacher for over 32 years both with undergraduates and post-graduate, he continued to take active interest in teaching all his life.

The Fellowship of the Indian Academy of Medical Sciences was conferred on him in 1961 and the Fellowship of the Royal College of Physicians (Edin.) in 1967.

A man of great personal charm and gentle manners, his death leaves a great void in the medical profession of the country. Not for long shall we see the like of him

—Arthur E. de Sa

Ann Natl Acad Med Sci (India), 13, 4, Oct.-Dec. 1977

Editorial

Child Nutrition

India along with many other developing countries has a young population, 42 per cent being under the age of 15 years and 17 per cent under the age of 5 years. The problems of infections and nutrition are great in this group particularly in children under 5 who are experiencing rapid growth and are therefore more vulnerable. Both mortality and birth rate are high. There is a rapid turn over, a new child replacing the old very quickly. Infant mortality is 120/1000 live births and is much higher in some rural areas. Almost half the deaths occur under the age of 5 years. Immediate causes of death are diarrhoeal disorders and respiratory diseases. However malnutrition is an important underlying cause in most cases. Thirty per cent of school children are malnourished. Out of 100 million preschool children, 3-4 million suffer from severe types of malnutrition, and probably one million die because of this every year. There is well documented interaction between nutrition and infections particularly so between protein energy malnutrition and diarrhoea. Diarrhoeal disease contributes significantly to malnutrition and in turn to death. More malnourished the child, more prone he is to serious complications and the clinical course of the disease is also more protracted.

In most developing countries levels of nutritional intake are low for the vast majority of the population. This particularly affects the vulnerable group of young children and pregnant and nursing mothers. Several surveys in different parts of India have shown that the nutritional intake between the ages of 1-5 years is usually much less than what is needed, the deficit being in the region of about 30 per cent. Only part of this is due to poverty and low purchasing power. Lack of knowledge about dietary requirements of the child and ignorance and prejudices contribute a great deal to malnutrition. Coupled with this are repeated infections due to poor environmental sanitation and unsatisfactory water supply and this has an adverse effect on the already poor level of nutrition.

Caloric and protien requirements at different ages.

Age group	*Body weight (Kg.)*	*Energy (Kcal)*	*Protein (g.)*
Birth to 6 months	3— 7	600	11
6 months to 1 year	7— 9	800	13
1 to 3 years	9—13	1200	18
4 to 6 years	15—17	1500	22
7 to 9 years	18—21	1800	33
10 to 12 years	23—28	2100	41

(The National Institute of Nutrition, 1972).

Actual and recommended diet intake of preschool children.

	Actual intake	*Recommended intake*
Cereals (g.)	147	150– 200
Pulses (g.)	16	40— 50
Leafy vegetables (g.)	4	50— 75
Other vegetables (g.)	14	30— 50
Fruits (g.)	7	40— 50
Milk and milk products (g.)	80	200
Fats and oils (g.)	4	20— 25
Flesh foods (g.)	4	30
Sugar and jaggery (g.)	5	30– 40
Calories (cal.)	758	1200--1300
Protein	19	18— 19
Iron (mg.)	6.9	17.5
Calcium (mg.)	193	450
Vitamin A (μg.)	220	350
Riboflavin (mg.)		0.7

(Sources : Nutrition Expert Group of ICMR, 1968).

In the past there has been a great deal of talk regarding protein deficiency leading to malnutrition with the result that several expensive high protein foods are being marketed and advertised. Even some of the international agencies were responsible in the past for distributing skimmed milk powder at various MCH and other centres. This was a hangover from the African experience where babies were weaned on to a completely carbohydrate diet, resulting in Kwashiorkor. In India, however, the existing dietary pattern of cereals and pulses cannot result in protein deficiency if adequate amount is eaten, since both are fairly good sources of proteins. By mixing different vegetable proteins with dissimilar amino acid pattern, the biological value will improve and thereby the protein will be better utilized by the body. Cereals such as wheat are deficient in lysine while pulses have a relative abundance of it. By combining the two, the chemical score of the protein in relation to the reference protein of egg (which has a score of 100) can be improved. Multimixes of this type are fortunately consumed traditionally in this country, but the habit should be further encouraged. The deficiency is of calories rather than of proteins and it is the total food that has to be increased rather than bothering about proteins. Extra proteins in the absence of required calories are used for energy rather than for tissue building.

Fortunately the practice of breast feeding is almost universal in India except amongst the so called educated women and the high socio-economic group. However in urban areas, the bottle is fast replacing the breast with disastrous results for the baby especially among the urban slum dwellers. The reasons for this shift to the bottle are not well understood although the pressure of advertising for commercial baby foods, the atmosphere of economic and social insecurity, sometimes misleading advice from doctors and nurses and other social and economical factors have been blamed. The medical profession often adopts a very casual attitude to breast feeding and at the slightest excuse the breast milk is replaced by bottle feeding. In the urban environment the bottle is offered even as early as the first or second month. Because of poor hygiene, this leads to diarrhoea and to malnutrition. Breast milk protects the child from infections not only because it is free from micro-organisms but also because it has many protective factors such as IgA, bifidus factor, lysozyme and lactoferrin. Human milk has the lowest solute load of all mammals particularly low sodium and proteins. Higher solute load of animal milk leads to water retention and raised blood urea levels. Breast milk is a richer source of polyenoic fatty acids similar to those of human central nervous system. Its high lactose content is metabolised to galactose which in turn is incorporated into galactolipids in the brain and spinal cord. The high lactose and the specific pattern of fatty acids seem to facilitate the rapid growth in size and complexity of the brain. So it is evident that there is a great need to protect and promote breast feeding and to study measures by which its downward trend can be prevented.

The addition of semi-solids and solids is late in most parts of India and once the breast milk becomes inadequate malnutrition sets in. The growth curves of Indian babies are excellent for the first 4 months but begin to flatten after that because of inadequate calories. Unfortunately due to ignorance, infection and malnutrition between the ages of 6 months to 2 years are attributed to teething and no remedial measures are adopted. With each infection the diet is further reduced ultimately leading to further malnutrition. Several surveys have shown that the severer forms of malnutrition are more common between the ages of six months to two years and almost 10-15 per cent babies suffer from 3rd degree malnutrition (weight below 60 per cent of the Harvard 50th percentile). For the first six months the baby is more or less protected because of breast milk. Once the breast milk becomes less and the mother has no knowledge of the amount of food the child needs, malnutrition sets in because the child during this period is completely dependent on his mother for feeding. Once he becomes more independent, and can grab food when hungry, the level of malnutrition becomes less. The aim should be that a child of one year should be eating more or less the family food with some modifications in the form of softening or mashing. It has to be emphasised that a child can be adequately nourished with the ordinary household food rather than any special, high priced food. Milk being a prestige food is indulged in more than necessary by the affluent and even the diluted version (due to high cost) preferred to solid food by the less affluent. A child of one year does not need more than half a litre of milk a day. The advice should be to give a mixture of cereals, pulses with some green vegetables, because of their vitamin A, and iron content. They also supply vitamin B, C and calcium. Addition of a little oil adds to the calories because fat is a concentrated source of energy. The quality of food can further be improved by better cooking methods, sprouting etc. Apart from the quantity, bulk of the Indian diet poses another problem. A small child may have to be fed several times a day instead of only 3 or 4 times. This too is not realised by the mother, and not even by the medical profession and the health auxiliaries whose interest and knowledge regarding various aspects of practical nutrition is meagre.

Since malnutrition and infections go together it would only be right to have a comprehensive programme for health and nutrition comprising curative, promotive and preventive measures, including nutrition and health education rather than spending energy, effort and time on nutrition supplement programmes, which in the way they are carried out, pay no dividends at all.

—SHANTI GHOSH

Ann Natl Acd Med Sci (India). 13,4, Oct.-Dec. 1977

Contribution of Meteorological Conditions in Malaria Transmission : A Multi-factorial Analysis of Malaria Cases†

B.L. Verma*, S.D. Verma** and R.N. Srivastava***

Department of Social and Preventive Medicine, M.L.B. Medical College, Jhansi, (U.P.)

Received for publication, November 27, 1976.

A statistical analysis of 4 years (1969-1972) malaria cases along with the metereological data of the same period of maximum and minimum temperatures, rainfall and relative humidity of Jhansi district, was carried out to establish the significance of these correlative factors in malaria transmission and also to develop a regression function in terms of these factors. Analysis revealed a positive partial correlation of malaria transmission with minimum temperature and relative humidity and a negative correlations with maximum temperature and rainfall. Such factors contributed about 80 per cent of the total sum of squares. Highest contributor being maximum temperature, followed by minimum temperature, relative humidity and then rainfall in the same order.

Introduction

Numerous studies, in recent years, over the epidemiology of malariology, to investigate the grounds of deficiency in its control, have been conducted (Scholtens **et al** 1972, Srivastava **et al** 1975 and Srivastava **et al** 1976 and 1977). Rao (1973) elicited that cumulative effect of many factors has resulted in malaria cases showing increasing trend year after year. Srivastava **et al** (1976) presented some observations on seasonal variations of malaria in Jhansi district indicating possibilities of perineal transmission in at least some pockets of the area. However, literature showing contribution of nature in the level of transmission of the disease has, yet, not been presented in precise terms. Study of contribution of nature in the transmission level of an arthropod-borne disease like malaria, is important in the epidemiology of the disease and in evolving suitable local strategy for its control.

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†Paper presented at the V-National Conference on Communicable Diseases, held at Jhansi during Feb. 12-14, 1976.

*Statistician cum Lecturer,

**Statistical Assistant, (Now, Statistic Dissemination Officer) State Planning Institute, U.P., Lncknow.

***Professor and Head of the department.

Malaria is a seasonal disease with definite monthly fluctuations in many parts of the world (Srivastava **et al** 1976). Variations in the level of transmission are determined by variety of interrelated factors. Such interrelated factors might be the favourable metereological conditions like maximum and minimum temperatures, relative humidity and rainfall.

The present study was designed with the objective to define the significance of metereological factors in malaria transmission level and to test the hypothesis that the transmission level of the disease in a region, in the presence of vector and malaria parasites, to a great extent, is the multitude of regional correlative factors, and so expressible by a multiple regression function. The analysis would also indicate the percentage contribution of these variables in the determination of malaria endemicity.

Material and Methods

A statistical analysis of 4 years (1969-1972) monthly malaria positive cases detected (the dates of positive cases were taken from the dates on which the slides were collected) in Jhansi district through active/passive surveillance, along with the metereological data of rainfall, relative humidity and maximum and minimum temperatures for the same period, obtained from Regional Metereological Centre, Lucknow, was carried out. For multi-factorial analysis monthly actual values of 5 variables for complete 4 years were used to enumerate absolute, multiple as well as partial correlation coefficients.

Analysis of variance, in the absence of any other guide line available for this type of study, was carried out by the technique used by Indrayan **et al** (1974). Hence each factor was assigned independent arbitrary scores according to the scheme shown in Table I. These scores for each of 4 factors were easily chosen as these factors were already quantitative. Multiple regression equation was developed on the points suggested by Sendecor and Cochran (1967). Significance of such regression and regression-coefficients was tested by usual 'F' and student-'t' statistics respectively.

Obsesrvations and Results

Monthly distribution of malaria positive cases has been shown in Table-II and graph of these cases has been presented in Figure-1.

Data in Table II (Figure 1) revealed an increasing trend of malaria cases year after year with minimum cases in the month of February and maximum during the months of September and October. Season during August to November was however, observed to be favourable for the transmission of the disease.

Table I. Showing scores assigned to the various factors.

Factors	SCORES ASSIGNED 1	2	3	4	5	6	7
Maximum Temp. (°C)	26—30	30—34	34—38	38—42	42+	—	—
Minimum Temp. (°C)	2— 7	7—12	12—17	17—22	22—27	—	—
Humidity (%)	20—30	30—40	40—50	50—60	60—70	70—80	80+
Rainfall (mm.)	0—40	40—80	80—160	160+	—	—	—

Table II. Showing monthly distribution of malaria cases in Jhansi district during 4 years (1969-1972)

Months	YEARS 1969	1970	1971	1972
Jan.	2	—	46	90
Feb.	—	—	13	56
March	4	6	13	145
April	3	13	56	368
May	9	22	76	423
June	29	39	137	303
July	14	121	664	351
Aug.	64	222	584	666
Sept.	377	187	1,046	1,052
Oct.	227	463	1,111	1,323
Nov.	55	380	720	388
Dec.	—	69	211	181
Total	784	1,522	4,677	5,346

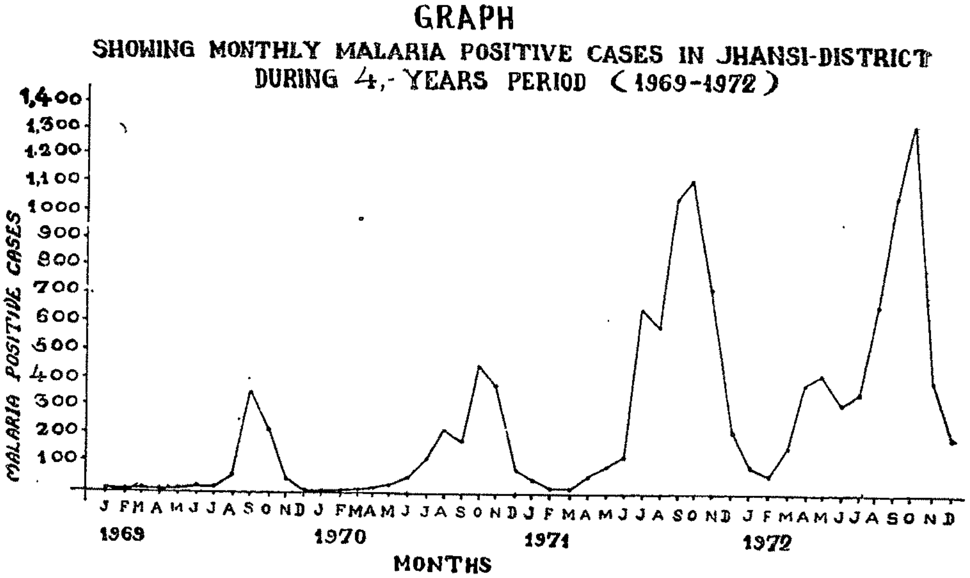

FIG. 1

Table-III gives the monthly metereological data of Jhansi district of maximum and minimum temperatures, relative humidity and rainfall during 4 year period (1969-1972).

Table III reflected that :-

(i) Monthly maximum temperature ranged from 26° C in the month of January to 46.3° C in the month of May.

(ii) Monthly minimum temperature ranged from 2.1° C in the month of February to 27.5° C in the month of June.

(iii) Monthly relative humidity at 0830 hrs. ranged from 21 per cent in the month of May to 87 per cent in the month of August.

(iv) Monthly rainfall ranged up to 587.3 mm. in the month of July.

Significance of each variable independently was attempted by working-out partial correlation coefficients. Table IV shows the values of partial correlation coefficients and their statistical significance.

Table IV revealed that malaria was exclusively positively correlated with minimum temperature and relative humidity but such correlation was negative with maximum temperature and rainfall. All these partial correlation coefficients were significant at one per cent level of significance.

Table III. Showing monthly maximum and minimum temperatures, humidity and rainfall in Jhansi district during the years 1969 to 1972

Months	MAXIMUM TEMPERATURE (°C)				MINIMUM TEMPERATURE(°C)				RELATIVE HUMIDITY (%) (0830 hrs)				RAINFALL (m.m.)			
	1969	1970	1971	1972	1969	1970	1971	1972	1969	1970	1971	1972	1969	1970	1971	1972
January	31.0	27.1	26.0	28.4	4.0	6.0	3.0	2.1	59	65	62	54	14.5	48.3	20.3	0.0
February	32.1	29.2	35.3	33.0	5.7	4.0	2.7	3.1	55	67	46	46	0.0	59.1	2.5	13.8
March	40.0	40.4	40.4	40.6	14.3	10.0	5.7	6.7	41	51	36	30	0.0	0.0	0.0	0.0
April	43.2	44.8	43.0	41.2	18.0	18.1	10.1	19.7	28	33	33	25	6.0	0.8	8.9	0.0
May	46.3	46.1	44.2	46.0	20.0	21.3	15.1	26.3	37	31	38	21	16.2	8.2	2.4	0.0
June	45.4	44.0	39.8	46.0	22.6	23.3	22.4	27.5	53	63	68	39	24.0	125.5	117.6	24.6
July	42.5	40.0	35.2	39.2	21.7	24.0	21.5	23.3	78	71	84	63	265.6	45.2	587.3	82.7
August	37.5	36.0	33.4	40.2	21.0	22.1	21.5	22.1	82	87	82	81	387.3	327.5	87.2	343.2
September	36.4	37.0	37.4	35.6	19.4	20.9	21.1	18.1	77	82	74	74	142.7	104.3	122.6	174.1
October	37.1	36.6	35.4	36.1	16.9	15.3	19.5	18.1	54	55	67	56	0.0	0.0	71.3	7.5
November	37.4	33.2	31.4	32.2	9.7	5.0	13.1	11.5	63	40	53	55	88.2	0.0	0.0	8.3
December	28.1	28.8	30.0	26.1	5.0	4.2	4.2	7.5	61	45	52	66	0.0	0.0	0.0	0.0

Table IV. Showing values of partial correlation coefficients* and their statistical significance

Factors	Partial correlation coefficients	Value of partial correlation at 43 d.f.	P-Value
Maximum Temp. (°C)	—0.4561	0.3870	<0.01
Minimum Temp. (°C)	0.5408	0.3870	<0.01
Humidity (%)	0.5923	0.3870	<0.01
Rainfall (mm.)	—0.5070	0.3870	<0.01

*Highest order partial correlation coefficients.

For the purpose of predicting malaria endemicity in terms of metereological variables, if vector and malaria parasites are present in the area, a multiple linear regression equation was developed.. In notations, such equation was:

$$Y = 1639.00 - 66.3465 X_1 + 55.0312 X_2 + 4.8714 X_3 - 0.1465 X_4.$$

where Y denoted expected malaria endemicity for specific values of metereological variables and X_1, X_2, X_3, and X_4 were the monthly actual values of maximum and minimum temperatures, relative humidity and rainfall respectively. Significance of such regression was tested by carrying-out analysis of variance shown in Table V.

Table V. Showing analysis of variance of multiple linear regression function as a test of significance

Sources of variation	d. f.	Sum of squares	M.S.S.	Value of Statistic-F	P—value
Regression	4	31,65,715	7,91,428.7	16.34**	<0.001
Deviation	43	20,83,053	48,443.1	—	—
Total	47	52,48,768	—	—	—

**Highly significant.

Table V shows that the linear multiple regression function obtained for malaria endemicity in terms of metereological variables, was highly significant. Such regression yielded a multiple correlation coefficient of 0.6756 which was again statistically highly significant ($F = 9.0219$, d. f. 4, 43, $P \angle 0.001$).

For the purpose of testing individual regression coefficients, analysis shown in Table-V was further extended to a comprehensive analysis. Table VI gives the regression coeffiicents, their standard errors and significance in multiple regression separately.

Table VI. Showing regression coefficients, their standard errors and significance in multiple regression.

Factors	Regression coefficients	Standard error	Student t	P—value
Maximum Temp. (°C)	—66.34648	11.5993	5.7199	<0.0001
Minimum Temp (°C)	55.54030	7.8796	7.0486	<0.0001
Humidity (%)	4.87135	3.6096	1.3496	>0.100
Rainfall (mm.)	—0.14751	0.39618	0.3733	>0.50

Table VI revealed that regression coefficients for maximum and minimum temperatures were highly significant but such coefficients for relative humidity and rainfall were not significant.

Contribution of these correlative factors for malaria cases was assessed by carrying-out factor specific analysis of variance. Table VII shows factor specific analysis of variance for malaria cases.

Table VII. Showing factors specific analysis of variance for malaria cases.

Factors	d.f.	Sum of squares	Percentage	M.S.S.	Value of Statistic —t.	P-value
Maximum Temp. (°C)	4	17,56,009	80.47	4,39,002	12.85	<0.01
Minimum Temp. (°C)	4	11,45,921		2,86,480	8.38	<0.01
Humidity (%)	6	9,16,994		1,52,832	4.47	<0.01
Rainfall (mm.)	3	4,04,681		1,34,894	3.95	<0.05
Residual	30	10,25,163	19.53	34,172	—	—
Total	47	52,48,768	100.00	—	—	—

Table VII shows that each factor was significant at one per cent level of significance except for rainfall which was significant at 5 per cent level. Analysis also indicated that studied metereological variables contributed about 80 per cent (80.47 per cent) of the total sum of squares for malaria cases.

Discussion

Since, in multiple analysis case, absolute correlation coefficient between any two variables, measures the degree of relationship, not eliminating the effect of other variables studied, and so, for retaining accuracy, partial correlation coefficients of highest order were worked-out. These coefficients were significantly negative for maximum temperature and rainfall but positive for minimum temperature and humidity. This indicated that increase in minimum temperature and relative humidity will result into the advancing trend of malaria cases but if rest of the two variables **viz.** maximum temperature and rainfall increase, the quantum of infection in the area will go down. Probably this can be explained by the fact that increase in rainfall and maximum temperature of the areas after a certain limit may result into the destruction of the mosquitoe-load.

For a disease like malaria which is absolutely seasonal, a linear multiple regression function will not provide optimal results and hence the obtained regression function is only grossly accurate. However, regression function was seen to be highly significant ($P<0.0001$). The function is also of practical utility and simple to handle as it gives the expected malaria endemicity in terms of metereological data, provided the vector and malaria parasites are already there in the region.

As remarked earlier, with the help of the factor specific analysis of variance (Table VIII), each factor was seen to be responsible in the transmission of malaria parasites since individual variations due to these factors were highly significant ($P<0.01$). Owing to the varying degrees of freedom, it was difficult to say about the percentage contribution of each factor exactly. However, these variables jointly contributed about 80 per cent (80.47 per cent) of the total sum of squares. Thus if, vector and malaria parasites are already there in the area, about 80 per cent malaria infection might be due to the favourable metereological conditions. Analysis also revealed that highest contributor, in the variation of the malaria infection, was maximum temperature followed by minimum temperature, relative humidity and rainfall in the same order.

The present study though highlights elaborately the effect of metereology on malaria transmission, yet, it has got certain limitations. The limitation of the study also lies due to the fact that statistical analysis carried out in this study is based upon a period of 4 years only, and thus, a fact, that any variable having seasonal variation will be associated with another, behaving in a similar manner, has been ignored.

A deeper and more detailed study through 'Time Series Analysis' is needed to establish the significance of these correlative metereological factors for malaria infection in a region.

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Dental Caries and Dental Fluorosis in School Children---A Community Survey in Rural Areas of Haryana.

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A high incidence of dental caries (58.5 per cent) and dental fluorosis (57.0 per cent) reported in 270 school children from an area with water supply containing high concentrations of natural fluorides (1 to 3mg/L). In contrast, children from a comparable community having drinking water of low fluoride content (0.3-0.5mg/L) were found to have a lower incidence of dental caries (34.0 per cent). Dental caries affected the second molar more frequently in children residing in high fluoride area. Children who had dental fluorosis were found to have significant incidence of dental caries (67.5 per cent) in comparison to those who did not have dental fluorosis (46.5 per cent). In the survey reported, protective role of fluorides in drinking water against dental caries was not evident.

Introduction

It is commonly believed that fluorides have a protective action against dental caries and fluoridation of drinking water supply reduces the incidence of dental caries (Dean, 1938, 1943). Mottled enamel or dental fluorosis is reported to develop only when the fluoride content of drinking water is high. In a study from Punjab incidence of dental fluorosis could be correlated with water fluoride level (Jolly **et al** 1969). Concentrations of fluorides in drinking water between 1 to 1.5 mg/L are considered beneficial in preventing dental caries with little or no risk of inducing dental fluorosis. Further, fluorotic teeth have been found more resistant to dental caries than normal teeth (Armstrong and Brekhus, 1938). Singh **et al** (1962) from India reported a very low incidence of dental caries in a highly endemic area of dental and skeletal fluorosis.

Results of rural survey in school children upon the prevalence of dental caries and dental fluorosis conducted in two different areas with high and low fluoride content of drinking water respectively are being presented in the paper in the context of above mentioned findings reported elsewhere.

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Clinical Material

Five hundred thirty-four school children, mostly males, 7 to 17 years of age (Table I) were examined for the presence of dental caries and dental fluorosis. The children were mostly of poor socio-economic status and were living in a comparatively undeveloped Bhiwani District of the State of Haryana on the outskirts of desert area. The survey included available children from the school located in two villages supplied with drinking water having distinct differences in fluorides content. Two hundred and seventy children were from the village with water drawn from wells or tubewells for drinking purpose having a fluoride content of 1 to 3 mg/L, while 264 children were from another village with its water supply from wells or tubewells containing only small amounts of fluorides ranging from 0.3 to 0.5 mg/L. The children had been living in their respective villages since birth and the water supply of the two villages had not changed during the past twenty years. The two groups of children were comparable in respect to age, sex, socio economic status, nutrition and dietary habits. They had hardly been exposed to synthetic sweets and had never been previously examined by a qualified dentist. Both the villages are shown in the 'Low caries area' in the geological map of dental caries as mapped out by Mc. Phail and Grainger in 1969.

Results

The prevalence (Table I) of dental caries was found to be high amongst the school children studied. Approximately, 46 per cent of the 534 children showed evidence of dental caries. A comparison of the results obtained from the two villages showed significant differences (Table II). A higher incidence of dental caries was present in children from the high fluoride area (58.5 per cent) as compared to the low fluoride area (34.0 per cent). So was the incidence of fluorotic mottling of the teeth (57.0 per cent) in high fluoride area. Various teeth involvement per child were also higher in high fluoride area than in low fluoride area. In high fluoride area 62 children had three or more carious teeth. The corresponding number in the low fluoride area was only six. Within the high fluoride area (Table II) children having evidence of dental fluorosis had a higher incidence of dental caries than those without such evidence and the teeth involvement per child was also significantly higher. An important observation concerned the pattern of tooth involvement in high and low fluorides area. While the first molar, the site of maximum frequency in caries, was commonly affected in the low fluoride area ; second molar was the common site of carious lession in the high fluoride area. This difference, previously unreported, was statistically highly significant (Table II). In the high fluoride area, children with mottled teeth showed more frequent involvement of the second molar by caries but the difference was statistically not significant. (Table III).

Table I **Dental caries and dental fluorosis (Age of the subjects charted in the two areas surveyed).**

Age in years	High fluoride area			Low fluoride area		
	No. of Children	D. caries	D. fluorosis	No. of Children	D. caries	D. fluorosis
7	15	7	3	13	5	—
8	11	6	8	15	7	—
9	18	10	7	26	6	—
10	32	20	22	35	13	—
11	30	18	19	30	9	—
12	40	22	25	40	11	1
13	32	24	18	35	14	—
14	30	20	18	37	10	—
15	28	12	16	20	7	—
16	19	10	8	13	5	—
17	16	9	10	12	3	—
Total	270	158	154	264	90	1

Table II **Comparison of incidence of dental caries and dental fluorosis in High and Low fluoride areas.**

Description	High fluoride area	Low fluoride area	Statistical significance
Total Children	270	264	
Children with dental caries	158(58.5%)	90(34.0%)	P<.001
Children with dental fluorosis	154(57.0%)	1(0.4%)	P<.0001
No. of carious teeth per child	1.33	0.55	P<.001
No. of carious 1st molars	132	40	P<.001
No. of carious 2nd molars	215		
Others	12	17	
No. of carious permanent teeth	352	136	
No. of carious milk teeth	7	9	
No. of children with one carious tooth	28	43	
No. of children with two carious teeth	68	41	
No. of children with three or more carious teeth	62	6	
Fluoride content of drinking water (10 samples)	1-3mg/L	0.3-0.5mg/L	

Table III **Incidence of dental caries amongst children with or without dental fluorisis in 'High fluoride area'.**

Description	Children with dental fluorosis	Children without dental fluorosis	Statistical Significance
Total children	154	116	
Children with dental caries	104(67.5%)	54(46.5%)	$P<.001$
Carious teeth per child	1.46	1.09	$P<.002$
Carious 1st molars	82	48	$P<.5$
Carious 2nd molars	138	72	
Other teeth (carious)	5	7	

Discussion

Although the effects of chronic fluorine toxicity on skeletal and dental tissues are well recognized, many countries are resorting to fluoridation of drinking water in the hope of limiting the incidence of dental caries. Fluorides are being added, for similar reasons, to various dentiferous preparations and are being advocated for local applications as well. The amounts of fluorides added to the water supply, admittedly have been small carrying almost no risk of chronic toxicity. The effects of these measures have been the subject of scientific papers on dental carries published recently (Jackson **et al** 1974 and Jenny, 1974).

Our observations in school children, exposed to moderately high quantities of fluorides in drinking water manifesting clinically as fluorotic mottling of teeth, showing a higher incidence of dental caries is of some significance. While it is possible for fluorotic pits to act as focal points for bacterial growth and food decay thereby inducing caries, the explanation does not seem likely in these children. One would have expected the teeth affected by caries to be also fluorotic which was not the case. Further, while fluorotic mottling of teeth was mostly seen on the incisors, dental caries commonly affected the molars.

Analysis of results of the small survey we have reported suggests that high concentrations of fluorides in drinking water supply had apparently failed to show the expected protective action against dental caries. From the neighbouring State of Punjab, Jolly and coworkers (1973) have also reported an incidence of 14-40 per cent of dental caries in a highly endemic area of dental and skeletal fluorosis. The safe optimum limit of fluoride in this country is in the range of 0.5 to 0.8 p. p. m. (Jolly, 1976).

It is not possible at this stage to explain the reasons for higher incidence of dental caries amongst the children drinking water of higher fluoride content as compared to those who were drinking water containing low concentrations of fluorides.

There were no apparent additional factors which could explain this difference. A possible clue might be in the observation that the carious involvement of teeth amongst children from 'High fluoride area' seemed to occur preferentially in second molar in contrast to the first molar which was involved in children from the 'low fluoride area'. Further work is needed to elucidate the significance of this finding.

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Medullary Carcinoma of Thyroid

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Medullary Carcinoma of the thyroid gland is a potential killer. It has a bizzare presentation. Its early recognition is possible in view of biochemical changes which precede its appearance. The clinical, biochemical and other diagnostic features of medullary carcinoma have been described alongwith a brief clinical review of a few cases.

Introduction

Medullary carcinoma of the thyroid gland (M.C.T.) is a tumour of the parafollicular or 'C-cells'. It comprises 3.5 to 10 per cent of all thyroid carcinomas (Gorlin **et al**, 1968). It is a potential killer and has a tendency to simulate certain behavioural characteristics of both papillary and poorly differentiated carcinomas of the thyroid (Davis, 1967). It tends to involve both lobes of the thyroid, metastasize into cervical nodes and distant sites : resist therapeutic measures other than surgery : be associated with other endocrine lesions like phaeochromocytoma and hyperparathyroidism ; and occur as an autosomal dominant characteristic in some families (Block **et al**, 1968).

Pathology

Macroscopically it is a solid tumour with uniformly grey or yellow grey cut surface and a clearly demarcated border. Microscopically the border is less distinct and engulfed thyroid follicles may be seen within the outer part of the tumour. The solid sheets and islands of cells, amyloid deposits, presence of binucleate cells, focal calcification and high incidence of cervical lymphnode metastases are characteristic histopathological features (Williams **et al** 1966). Amyloid deposits are found within the tumour and stain typically with congo red, methyl violet and thioflavin T.

Clinical Features

The initial clinical presentation of the tumour is usually indistinguishable from that of other benign and malignant causes of thyroid enlargement (Baylin, 1974). It exhibits a familial incidence in over 50 per cent cases (Rasmussen, 1974) where the pattern of inheritance is autosomal dominant. The clinical features may be divided into following four groups :-

1. **Neck swelling and local effects :** The cervical swelling may be due to the thyroid enlargement with adenopathy or to adenopathy alone. The enlarged thyroid may be in the form of a unilateral enlargement, a diffuse goitre, or a multinodular goitre : less often there may be only one or more palpable nodules in the thyroid that appears otherwise normal. A clinical diagnosis of carcinoma can be made in about 50 per cent patients by its hard consistency, fixity and cervical lymph node metastases. Sometimes there is severe local tenderness which may lead to a diagnosis of thyroiditis. Occasionally the growth may result in dyspnoea, dysphonia or dysphagia (Muller, 1969). Lymphatic or direct spread to the mediastinum is common and x-rays may show areas of calcification in the neck or anterior mediastinum. Sometimes the primary focus may stay dormant and the patient may present with the metastatic involvement of the lungs, liver and bones.

2. **Mucosal neuroma syndrome and associated features** : Multiple mucosal neuromatosis (M.M.N.) usually involving the eyelids, lips, tongue and oropharyngeal mucosa, autonomic ganglioneuromatosis, diverticulosis, megacolon, poorly developed musculature, cafe-au-lait spots and various other anomalies such as sugar loaf skull, pectus excavatum, scoliosis, high arched palate, decaying teeth with poor enamel, absent facial and axillary hair, marfanoid habitus and arachnodactyly may also be seen with M.C.T. (Williams and Pollock, 1966).

3. **Multiple-endocrine-adenomatosis (M.E.A. Type II) and associated features :** The familial form of the tumour usually occurs as Sipple's syndrome or M.E.A. type II (Sipple, 1961) where it is associated with phaeochromocytomas and are bilateral in 75 per cent cases and may be extra-adrenal (Williams, 1965). It is not clear if the association of parathyroid hyperplasia/adenoma is compensatory to the increased circulating calcitonin levels (C.T.), or genetically determined (Williams, 1967 ; Meyer and Bari, 1968). Serum calcium (Ca) levels are usually normal. Nephrocalcinosis and renal calculi may be present at times even when the urinary Ca and phosphorus (P) are normal.

4. **Humoral syndromes resulting from ectopic secretions of Hormones and enzymes :** The tumour cells secrete increased amounts of C.T. and sometimes also prostaglandins (E2 and F2) (Williams **et al**, 1968 ; Lancet, 1968), corticotrophin (A.C.T.H.) or A.C.T.H.—like peptides (Williams **et al**, 1968) ; serotonin (5-hydroxytryptamine (Moertel **et al**, 1965) ; dopa decarboxylase (Atkins **et al**, 1973) ; histaminase (Baylin

et al, 1970) ; and perhaps melanocyte-stimulating-hormone (M.S.H.)—like peptides (Cunliffe **et al**, 1970). Diarrhoea occurs in about 30 per cent cases (Barrowman **et al**, 1975). It may be intractable and profuse leading to weightloss, gross fluid and electrolyte depletion and alkalosis. A combination of hormones may be responsible but recent studies support a major role for the prostglandins (Mecklenburg **et al**, 1964 ; O'Higgins 1973). Occasionally Cushing's syndrome results from the ectopic production of A.C.T.H.—like peptide by the tumour. When associated with adrenal medullary tumours, paroxysmal hypertension, headache, visual disturbances, chest pain and discomfort, flushing of the face and excessive sweating may be the presenting features.

Ten cases of M.C.T. seen over the last six years are described in brief (Table). **Diagnositic investigations :** The following investigations are helpful in reaching an early and definite diagnosis.

Biochemical investigations : The parafollicular or 'C' cells of the thyroid produce C.T. (normal basal plasma C.T. less than 0.1 to 0.38 ng./ml. ; during calcium infusion there is a 2 to 3 fold rise, but levels never exceed 0.55 ng ml). C.T. is increased in cases of M.C.T. It is present in high concentration in the tumour mass, amyloid deposits and metastases. It is best estimated during stimulation tests by intravenous infusions of calcium or magnesium or intravenous injections of glucagon, gastrin and pentagastrin (Tashjian **et al**, 1970 ; Melvin **et al**, 1971, Melvin **et al**, 1972 ; Hennassy **et al**, 1973). Oral administration of alcohol also increases C.T. (Cohen **et al**, 1973). Alcohol is absorbed very rapidly from the gut, and its action on C.T. levels may be direct or through the gut hormones. Serum Ca, P, alkaline phospatase (A.P.) and parathormone (P.T.H.) should be estimated at the same time as C.T. Serum Ca is usually normal presumably because the increased C.T. levels may be compensated by parathyroid hyperplasia or by adenomas secreting P.T.H.

Serum histaminase activity : M.C.T. is known to secrete histaminase. This enzyme catalyzes the deamination of histaminase in tissues. It is produced in large amounts by the placenta. The serum levels of histaminase are high during pregnancy and after intravenous heparin. High levels are found in the kidney and ileum but concentrations are low in other normal human tissues. M.C.T. is the only neoplasm to have high histaminase activity (Baylin **et al**, 1972). The serum activity is increased when metastases have occurred and is highest in the presence of pulmonary metastases (B.M.J. 1973). Thus estimation of serum histaminase activity is useful in the preoperative detection of metastases as well as the search for residual or recurrent tumour after thyroidectomy.

Standard thyroid function tests : These are usually normal but since the M.C.T. does not concentrate iodine, a thyroid scan may show areas of reduced uptake. If the tumour is too small to be detected by careful palpation the scan is usually negative.

24-hour urinary catecholamines and their metabolites : These should be estimated to screen all patients with M.C.T. for phaeochromocytoma.

Radiological investigations : Skeletal survey may show chondrocalcinosis of the knees and wrists. Bone metastases are primarily osteolytic, but some sclerotic and lytic—sclerotic deposits may also be present. The cervical region and chest x-ray films may show areas of calcification in the thyroid mass, tracheal shift, mediastinal enlargement and pulmonary metastases. Tumour calcification is seen in less than 40 per cent cases, but the finding of thyroid calcification is not diagnostic of medullary carcinoma since other thyroid tumours or even multinodular goitres may calcify. The pattern of calcification in other tumours may show a faint homogenous density, the psammomatous calcification, whereas in M.C.T. large discrete calcified areas may be observed. Pulmonary metastases are most prominent in the mid lung fields and are of interstitial nodular type with a fibrotic appearance. Metastatic calcification may also be present.

Discussion

Horn (1951) was the first to describe it as a morphologically distinct type of thyroid carcinoma. Laskowski (1957) called it 'Carcinoma thyroideum hyalinium', but as a distinct clinicopathological entity it was first recognised by Hazard **et al** (1959) who gave it the present name. The distinctive solid character of M.C.T. led Williams **et al** (1966) to suggest its origin from the parafollicular (light, clear) cells of Nonidez (1932). Since the discovery that C.T. is produced by these cells, they have been known as the C-cells (Pearse, 1966). These are distributed in a non-homogenous manner in normal human thyroid. The tumour is usually located between the lower 2/3 and the upper 1/3 of the thyroid lobes. A multicentric but anatomically restricted C-cell hyperplasia syndrome may precede the true M.C.T. (Wolfe **et al**, 1973). The sequential estimation of C.T. response to calcium infusion in patients at risk for hereditary M.C.T. may allow detection of a premalignant type of parafollicular cell hyperplasia providing for even earlier surgical intervention.

Eisenburg and Wallerstein (1932) were the first to draw attention to the association of M.C.T. and phaeocromocytoma. This association has also been emphasized by Sipple (1961), who suggested a hormonal interrelation. Ljungberg **et al** (1967) noted that sections of M.C.T. treated with special stains showed tinctorial characteristics of chromaffin tissue. They suggested that the syndrome was a familial chromaffinomatosis.

M.C.T. resists all therpeutic measures other than surgery. A total thyroidectomy along with regional lymph nodes resection appears to be the most appropriate form of therapy. In view of the frequent involvement of the mediastinum which may represent a further primary tumour rather than metastases, prophylactic thymectomy has been advised by some (B.M.J. 1968). M.C.T. does not respond significantly to radioiodine therapy, external radiation, exogenous thyroid hormone or antitumour drugs. In some cases radiation therapy may prove useful for palliation of bone pain. Postoperative follow up should include periodic chest skiagrams, metastatic bone surveys, bone scans and liver function tests.

Familial M.M.N. syndrome is inherited as a dominant with almost complete penetrance. As it is invariably associated with M.C.T. which may result in death at an early age, prophylactic thyroidectomy should be carried out. In sporadic cases of M.M.N. syndrome, spontaneous mutation seems to be relatively frequent. This maintains the constant gene pool in the population.

First degree relatives of patients with M.C.T./M.M.N. syndrome should be screened annually for raised C.T. levels and phaeochromocytoma (flow chart). Both basal and post stimulation C.T. levels should be estimated. Prophylactic thyroidectomy may have to be considered in those with a familial incidence and increased C.T. values.

Conclusion

M.C.T. may occur sporadically or on a familial basis with autosomal dominant inheritance. It has a bizarre mode of presentation due in part to the different humoral agents which it may secrete. Total thyroidectomy is the only effective therapy. Prophylactic thyroidectomy or even thymectomy may be justified in selected group of patients. Detection of raised C.T. levels is the best method of reaching an early diagnosis since the plasma C.T. is raised even before the clinical appearance of M.C.T.

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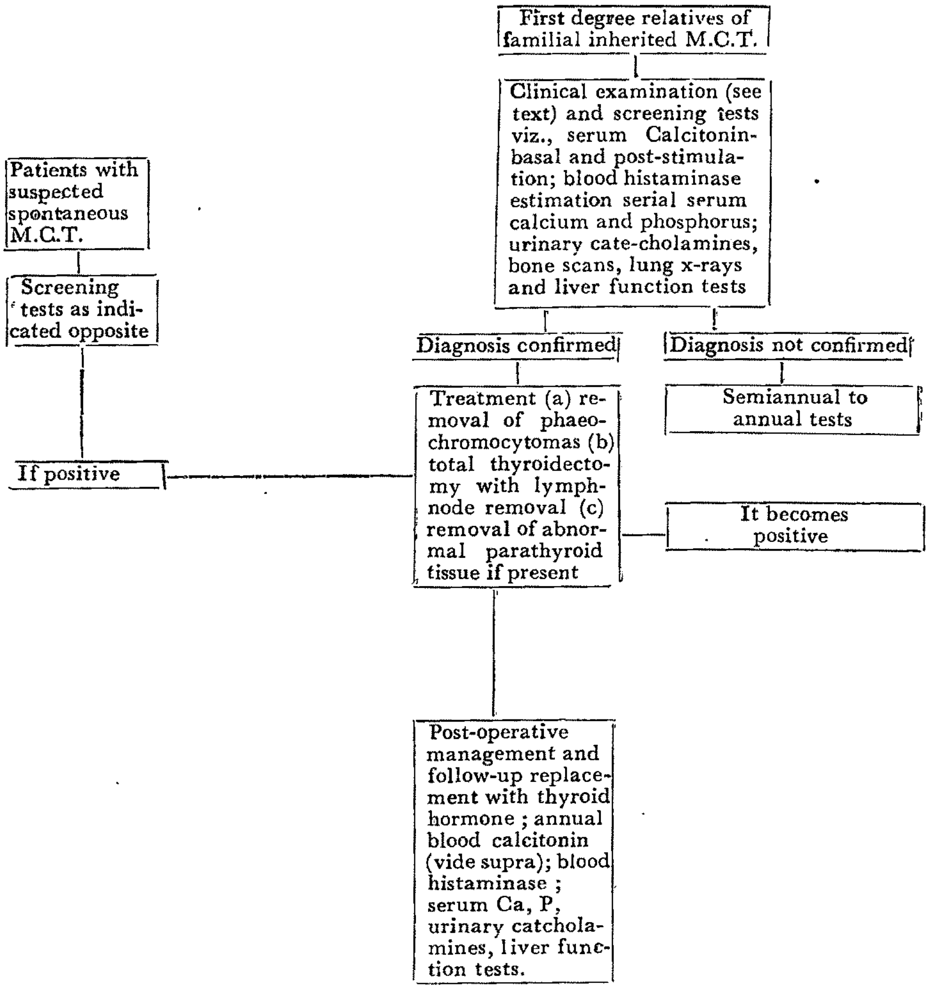
First degree relatives of familial inherited M.C.T.
Clinical examination (see text) and screening tests viz., serum Calcitonin-basal and post-stimulation; blood histaminase estimation serial serum calcium and phosphorus; urinary cate-cholamines, bone scans, lung x-rays and liver function tests
Patients with suspected spontaneous M.C.T.
Screening tests as indicated opposite
Diagnosis confirmed
Diagnosis not confirmed
Treatment (a) removal of phaeochromocytomas (b) total thyroidectomy with lymph-node removal (c) removal of abnormal parathyroid tissue if present
Semiannual to annual tests
If positive
It becomes positive
Post-operative management and follow-up replacement with thyroid hormone ; annual blood calcitonin (vide supra); blood histaminase ; serum Ca, P, urinary catcholamines, liver function tests.

Flow chart indicating approach to diagnosis and management of medullary thyroid carcinoma (M.C.T.)

Table : Medullary Carcinoma of Thyroid (M. C. T.)

Serial No.	Patients' particulars	Subjective complaints	Objective features	Diagnosis	Treatment	Progress and outcome
(1)	(3)	(3)	(4)	(5)	(6)	(7)
			Group 'A' Patients (with Neck Swelling)			
1.	43 years Female	Thyroid Swelling	Moderate goitre. Enthyroid. Thyroid histology confirmed M.C.T.	M. C. T.	Total thyroidectomy	Six year later multiple nodules in the neck and mediastinum appeared. Total excision carried out. M.C.T. confirmed. Died nine years after operation.
2.	61 years Female	Thyroid swelling. Skin nodules over chest and abdomen	Goitre axillary lymphadenopathy. Confirmatory histopathology of skin nodules	M.C.T. with metastasis in skin and lymphnodes	—	Died within year of the diagnosis.
3.	23 years Female	Thyroid nodule	Small goitre with a thyroid nodule	M. C. T.	Total thyroidectomy	Maintained on eltroxin replacement therapy. Developed recurrence after 14 years and presented with goitre, features of mediastinal compression and bilateral chylous pleural effusion.
4.	62 years Male	Thyroid swelling (Lt)	Unilateral goitre with cervical lymphadenopathy	M. C. T.	External irradiation with cyclophosphamide therapy	Five years later developed loose motions, widening of superior mediastinum and tender hepatomegaly. Cyclophosphamide therapy was re-instituted but no permanent relief and died after 8 years.

(1)	(2)	(3)	(4)	(5)	(6)	(7)
			Group 'A' Patients (with Neck Swelling)			
5.	46 years Female	Goitre (Rt) with regional lymphadenopathy	Thyroid swelling (Rt) Cervical lymphadenopathy	M. C. T.	Total thyroid ectomy	Well maintained with eltroxin and oral calcium, Age 55 years,
			Group 'B' Patients [Multiple Mucosal Neuromatosis (MMN)]			
1.	3 days Female	Poor feeding, repeated vomiting, failure to thrive	Generalised hypotonia, prominent lips, a small nodule on the tongue. Neuromatous malformation in the sub mucosal plexuses of rectal biopsy.	M.M.N. with M.C.T.	Prophylactic total thyroidectomy at one year of age	Alive 3½ years. Maintained on eltroxin. Has generalised hypotonia. Poor head control. Is unable to sit.
2.	6 years Male	Generalised hypotonia. Stunted Growth	Generalised hypotonia. Proximal myopathy. Thick lips, large jaw. Neuromas on tongue and lips.	M.M.N. with M.C.T.	Prophylactic total thyroidectomy	14 years old. Maintained on eltroxin. Complains or poor erection (autouomic disturbanccs).
3.	19 years Female	Acne, goitre, pigmentation face, hands and feet	Diarrhoea, recurrent flushes, thick lips, multiple neuromas tongue and upper eye lids, high arched palate, pes cavus, kyphosis, marfanoid features, proximal muscles weakness. Head nodular goitre with lymphadenopathy	M.M.N. with M. C. T. Myopathy due to succinic dehydrogenase defect	Total thyroidectomy	Died after a year

(1)	(2)	(3)	(4)	(5)	(6)	(7)
Group 'C' Patients [Multiple—Endocrine—Adenomatosis (M.E.A. Type II)]						
1.	49 years Female	Myxoedema	Palpitation, mass right lumbar region (back), secondary hepatic deposits	Phaeochromocytoma (Rt). M.C.T. with metastatic hepatic involvement	Adrenalectomy (Rt) Periodic check up.	
Group 'D' Patients (Humoral Syndomes)						
1.	53 years Male	Watery diarrhoea	Thyroid nodule (Rt)	Medullary carcinoma	Thyroidectomy followed by external irrradiation, nutmcg and indomethacin therapy.	56 years old. Well maintained on eltroxin.

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Studies on Human Transplacental Transfer of 2-Mercaptoethanol Resistant and Sensitive HI Antibodies of Influenza and Arbovirus

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Sixty four pairs of mother-cord sera were tested for the presence of haemagglutination inhibition (HI) antibody against influenza A_2-Hongkong, 68 (A_2/HK/68) and influenza B-Coonoor/70 (B-Coon/70) and against group B arboviruses—Japanese encephalitis (JE), West Nile (WN), dengue—I (DEN-1), dengue II (DEN-2), dengue III (DEN-3), dengue IV (DEN-4) and group A arboviruses--Chikungunya (CHIK) and Sindbis (Sind), before and after 2-mercaptoethanol (2-ME) treatment. 89.06 per cent of the paired sera were positive for influenza A_2/HK/68 and 74.69 per cent for B/Coon/70 HI antibodies, while 90.42 per cent showed one or more of group B-arboviruses and 18.75 per cent and 1.56 per cent for CHIK and Sind respectively. After 2-ME treatment, there was more than four-fold reduction in titre in influenza strains A_2/HK/68, B/Coon/70 and group A and group B arboviruses HI antibodies in certain sera showing the recent infection.

Introduction

Placental transmission of antibodies had been reported in human beings and animals, in various virus infections, namely, pox viruses (Rao **et al**, 1969, Saha **et al**, 1973 and Takashi **et al**, 1973), Poliomyelitis virus (Agarwal **et al**, 1971), arboviruses (Gregg **et al**, 1941 and Hale and Lee, 1954), Western equine and St. Louis encephalitis viruses (Longshore, 1959), Influenza A_2/HK (Mantyjarvi **et al**, 1970), rubella (Inouya and Kono, 1972) and for pox and arboviruses (Sarkar **et al**, 1973). It is interesting to know the nature of antibody that has been transferred through the placenta of human being in the case of Influenza A and B and Group A and Group B arboviruses infections. Hence, the distribution of ME sensitive (19 S) and resistant (7 S) antibodies to viruses (influenza and arboviruses) have been studied with a view to determine evidence of intra-uterine infection of these viruses as well as transplacental transfer of maternal antibodies.

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Material and Methods

Sera Samples : Five to eight ml. of the blood samples of mother-cord pairs were collected from the veins of women admitted for delivery and from the umblical cord of the new born babies at the Raja Sir Ramaswamy Mudhaliar lying-in Hospital, Madras 1. Sera were separated and stored at -20°C.

A total of 64 pairs of mother-cord sera were collected during the later months of 1972 and the first two months of 1973. These sera were tested for the antibodies against the Group A and B arboviruses and influenza A_2/HK/68 and influenza B/Coon/70 strains.

Arbovirus haemagglutinating (HA) antigens and standard hyperimmune sera for dengue types, (DEN-1, DEN-2 and DEN-3) JE, WN, CHIK and Sind viruses were procured from the Virus Research Centre, Poona and the influenza HA antigens and hyperimmune sera for influenza A_2/HK/68 and influenza B/Coon/70 were obtained from the Pasteur Institute, Coonoor, S. India.

Haemagglutination Inhibition (HI) test for influenza and arboviruses :

Influenza : HI test was performed after treating the sera with 0.4 per cent trypsin to remove the non-specific inhibitors according to the methods of Thind (1971) and use of making four units of antigens and equal volume of 0.5 per cent fowl RBC. The titre was read after 45 min. at room temperature.

Arbovirus : HI tests were performed for both the maternal and cord blood against the above mentioned arbovirus antigens in microtitre 'U' plates as per the method of Clarks and Casals (1958) after Kaolin treatment and absorption with goose RBCS. The sera were then considered as 1 : 10 dilution and used directly for the test. Half the quantity of the sera treated for both influenza and arboviruses were used for the studies with 2-ME treatment.

Mercaptoethanol treatment : Each serum sample after treatment with Kaolin or trypsin was mixed with an equal volume of 0.2M solution of 2-ME in phosphate buffered saline (PBS : 0.1M at PH 7.6) and incubated at 37°C for one hour (Inouye and Kono, 1972).

Results

Influenza : A titre of 1 : 20 or more was considered as positive. Out of 64 pairs of sera, 62 pairs were tested against influenza A_2/HK/68 and B/Coon 70. HI antibodies ranged from 1 : 20 to 1 : 2560 against A_2/HK/68 in 57 pairs (89.06 per cent) and from

1 : 20 to 1 : 1280 against B/Coon/70 in 51 pairs (74.69 per cent). On further analysis of the data, it was found that the findings can be divided into four categories as follows :-

(i) More in child than in mother in 27 pairs (42.7 per cent) in B/Coon/70 and 23 pairs (35.94 per cent) in A_2/HK/68 influenza.

(ii) More in mother than in child in 11 pairs (17.1 per cent) in B/Coon/70 and 26 pairs (40.6 per cent) in A_2/HK/68 influenza.

(iii) Titre equal in both mother and cord blood in 13 pairs (20.3 per cent) in B/Coon/70 and in 8 pairs (12.5 per cent) in A_2/HK/68 influenza.

(iv) Antibody absent in both mother and cord blood sera in 13 pairs (20.3 per cent) in B/Coon/70 and in 7 pairs (10.9 per cent) in A_2/HK/68 influenza. The results are shown in Table I.

Arboviruses : Out of 64 pairs 58 pairs were positive (HI titre more than 1 : 20) which ranged from 1 : 20 to 1 : 1280 against group B arboviruses and in 12 pairs (18.75 per cent) against CHIK (ranged from 1 : 20 to 1 : 320) and one pair (1.56 per cent) 1 : 80 HI titre against Sind virus of Group A arboviruses.

(i) Antibody titre was found more in cord blood in 18 pairs (28.1 per cent) to group B and in 4 pairs (6.2 per cent) to group A arboviruses.

(ii) Antibody titre was found more in mother blood in 25 pairs (39.0 per cent) to group B and in 5 pairs (7.8 per cent) to group A arboviruses.

(iii) Antibody titre was equal in both the mother and cord blood in 23 pairs (35.9 per cent) to group B and in 3 pairs (4.7 per cent) to group A arboviruses.

(iv) There was no antibody in 6 pairs (9.4 per cent) against group B arboviruses and in 52 pairs for CHIK (81.3 per cent) and in 63 pairs (98.4 per cent) for Sind of group A arboviruses.

The pattern of distribution of HI antibody for each antigens namely DEN-1, DEN-2, DEN-3, JE, WN, CHIK and Sind with respect to mother and cord paired sera has been tabulated in Table I.

Geometric mean titre for the positive sera of HI arboviruses and influenza antibodies of mother and cord pairs are calclulated and tabulated in Table II.

Table I. The distribution of antibody against influenza and arboviruses in the mother and cord sera

	ARBOVIRUSES Group B										Group A				INFLUENZA A$_2$/HK/68		B/Coon/70	
	DEN-1		DEN-2		DEN-3		JE		WN		CHIK		Sind					
	a	b	a	b	a	b	a	b	a	b	a	b	a	b	a	b	a	b
Antibody titre more in child than in mother sera	15 (23.5)	10	16 (25.0)	7	18 (28.1)	6	17 (26.6)	8	17 (26.6)	4	4 (6.25)	1	—	—	23 (35.9)	14	27 (42.2)	—
Antibody titre more in mother than in child sera	25 (39.0)	15	21 (32.8)	15	15 (23.5)	8	17 (26.6)	8	18 (28.1)	10	5 (7.8)	4	1 (1.6)	1	26 (40.6)	12	11 (17.2)	6
Antibody titre equal in mother and child	8 (12.5)	—	11 (17.2)	—	21 (32.8)	—	22 (34.3)	—	23 (35.9)	—	3 (4.7)	—	—	—	8 (12.5)	—	13 (20.3)	—
Antibody titre in mother and child sera Nil	16 (25.0)	—	16 (25.0)	—	10 (15.6)	—	8 (12.5)	—	6 (9.4)	—	52 (81.35)	—	63 (98.4)	—	7 (10.9)	—	13 (20.3)	—
Total pairs of sera studied.	64	—	64	—	64	—	64	—	64	—	64	—	64	—	64	—	64	—

Note : Figures in bracket are the percentages a = One or two or four-fold or more antibody titre.
b = Four-fold or more difference in antibody titre.

Table II. Geometric mean titres of HI arboviruses and influenza antibody of mother and cord pairs before 2ME Treatment

Type of sera	Inf. A	Inf. B	DEN-1	DEN-2	DEN-3	JE	WN	CHIK	Sind
Mother blood	G.M.=218.5 Sd.=±0.5141 Total+ve=47	G.M.=63.04 Sd.=±0.4095 Total+ve=32	G.M.=128.3 Sd.=±0.5315 Total+ve=44	G.M.=99.13 Sd.=±0.5023 Total+ve=42	G.M.=214.4 Sd.=±0.3125 Total+ve=48	G.M.=144.1 Sd.=±0.4544 Total+ve=53	G.M.=137.9 Sd.=±0.5236 Total+ve=56	G.M.=79.98 Sd.=±0.4726 Total=9	G.M.=80.00 Total+ve=1
Cord blood	G.M.=191.4 Sd.=±0.4849 Total+ve=54	G.M.=88.88 Sd.=±0.4525 Total+ve=46	G.M.=114.1 Sd.=±0.1077 Total+ve=30	G.M.=73.35 Sd =±0.4820 Total+ve=40	G.M.=176.3 Sd.=±0.5031 Total+ve=50	G.M.=138.1 Sd.=±0.5092 Total+ve=52	G.M.=133.2 Sd.=±0.4790 Total+ve=53	G.M.=47.56 Sd.=±0.3506 Total+ve=8	Nil Nil Nil

But when the geometric mean was calculated on total 64 sera it was 52.35, 10.97, 28.15, 20.42, 55.88, 59.94, 74.33, 1.99 and 0.11 for influenza A, B, DEN-1 DEN-2, DEN-3, JE, WN, CHIK and Sind respectively for mother blood and 97.29, 34.78, 17.94, 14.65, 56.87, 54.84, 59.58, 1.68 and nil in Sind for cord blood.

2-ME treatment : As the 19S type of antibody is sensitive to 2-ME treatment, it was reduced unlike 7S antibodies. It was found that

(1) two to four-fold or more reduction of antibody titre was present in both maternal and the corresponding cord in 13 pairs in the influenza A_2/HK/68 and in 8 pairs in influenza B/Coon/70.

(2) two to four-fold or more reduction was found only in maternal and not in cord blood sera in 13 pairs of influenza A_2/HK/68 antibodies and in 12 pairs of influenza B/Coon/70 antibodies.

(3) no reduction was found either in maternal or cord blood sera in 24 pairs in influenza A_2/HK/68 and 30 pairs in influenza B.

(4) two to four-fold or more reduction was found only in child and not in maternal blood in 12 pairs of influenza A_2/HK/68 antibodies and 12 pairs of influenza B/Coon/70 antibodies.

In the same way, the pattern of reduction by treatment with 2-ME in the case of arboviruses with respect to each antigens, namely DEN-1, DEN-2, DEN-3, JE, WN, CHIK and Sind in mothers and cord blood as pairs are presented in Table III. The results after treatment with 2-ME, separately for maternal blood, and the cord blood, for the inflenza and arboviruses antigens are shown in Table IV.

Discussion

Our study corresponds with the result of Sarkar **et al** (1973) regarding the data on the percentage of sera showing equal antibody titres in both mother and cord blood in group B arboviruses and fall of antibody titre in the cord blood serum.

Our study also supported the findings of Mantyjarvi **et al** (1970) regarding influenza A_2/HK antibody titre. But in case of influenza B/Coon/70, the antibody titre is more in children than the mothers in 27 cases (42.18 per cent) less in children in 11 cases (17.18 per cent) and equal in mother and cord in 13 cases (25.31 per cent). It can also be noted that in the present study, the antibody titre is more in the case of mother than the child before the 2-ME treatment except in influenza B/Coon/70. In the case of the cord blood the macromolecular sized antibody namely the 19S may not be able to pass through the placental barrier unlike in rabbits where 19S can

Table III. Distribution of Influenza and Arbovirus antibody after 2 ME treatment in both mother and cord sera as pairs.

	INFLUENZA				ABROVIRUS														
	A		B		DEN-1		DEN-2		DEN-3		JE		WN		CHIK		Sind	
	a	b	a	b	a	b	a	b	a	b	a	b	a	b	a	b	a	b
1. Reduction present both in mother and child sera	13	3	8	3	10	4	0	0	15	5	12	2	11	2	1	1	0	0
2. Reduction only in mother and not in child sera	13	11	12	4	12	8	14	1	9	3	6	1	7	3	4	3	1	0
3. Reduction only in child and not in mother sera	12	2	12	6	11	7	5	1	8	2	9	5	4	1	3	0	0	0
4. Titre absent both in mother and child sera	24	0	30	0	25	0	39	0	26	0	31	0	36	0	50	0	57	0
5. Could not be done	2	0	2	0	6	0	6	0	6	0	6	0	6	0	6	0	6	0
6. Total pair of sera tested	64	0	64	0	64	0	64	0	64	0	64	0	64	0	64	0	64	0

a = One to fourfold or more reduction

b = Fourfold or more reduction.

Table IV. 2-ME treatment of mothers cord sera for arboviruses and influenza antibodies.

	Arboviruses							Influenza	
	DEN-1	DEN-2	DEN-3	JE	WN	CHIK	SIND	A_2HK/68	B/Coon/70
Two to four-fold reduction of titre present	*24/*20	13/5	20/25	20/20	19/20	4/4	0/0	26/25	18/17
Reductinn of antibody titre absent or same	35/38	46/53	37/33	39/38	40/38	55/54	59/58	33/32	41/40
Reduction of titre could not be studied	5/6	5/6	5/6	5/6	5/6	5/6	5/6	5/7	5/7
Total pairs	64	64	64	64	64	64	64	64	64

* mother sera

** cord blood sera

pass probably through the splanchnopleur (Shek and Dubiski, 1975). Hence both the 19S and 7S antibodies may be present in the case of mother. This also complied the study of Carey **et al** (1968) in Vellore (Tamil Nadu) where the high titre in the case of mother for group B arboviruses was due to the recent infection. While in the case of mother, whose antibody titre is equal to that of the cord blood the infection may be of past and the antibody involved may be of 7S type which can easily pass through the placenta from the mother to the cord. In these cases, the infection may be of past one only in the mother. This again is in accordance to the work of Hale and Lee (1954) for the JE neutralising antibody and Longshore **et al** (1959) for the CF and neutralising antibodies for the Western Equine and St. Louis encephalitis viruses.

Another feature of the present study was that in the case of DEN-2 and influenza B/Coon/70 the reduction of antibody (2-ME sensitive -19S) titre was less in both the mother and the cord after treatment with 2-ME, showing that the infection was of very past only **i.e.** during the early life of mothers.

Even though there were reductions in the case of influenza A_2/HK/68, and influenza B/Coon/70 in HI antibody titre after the 2-ME treatment in case of the cord blood indicating that the infection could be of in utero, none of the 64 children had shown any abnormalities, inspite of the report of congenital deformities produced by the influenza virus infection (Coffey and Jessop, 1963). Similarly, the present study indicated the infection by group B and A arboviruses in some mothers and there were no congenital abnormalities by these viruses infections during pregnancy as it was reported for other virus like rubella (Gregg, 1941), Coxsackie (Brown and Karunas, 1972) and cytomegalovirus (Haymaker **et al**, 1954).

In the case of CHIK antibody, it had been seen that out of 64 pairs (maternal--cord sera pairs), 12 pairs (18.75 per cent) had antibody in both the mother and cord sera. After 2-ME treatment, there was reduction in the titre in 4 pairs only in mother and not in child which clearly shows recent infection by CHIK. In these 4 pairs, the HI antibody titre was 1 : 320 in the maternal blood and there was no HI antibody in these 4 cord blood sera. The titre in mother blood was reduced after treatment with 2-ME which clearly shows that the antibody involved may be of 2-ME sensitive (19 S type) and due to its macromolecular size it was not transferred through the placenta. In another one pair, reduction was present in both mother and child sera which shows the infection during the gestation period.

In the present study the sera were not treated with acetone since as per Inouye and Kono (1972) acetone treatment causes aggregation of antibodies especially for the analysis of the classes of HI antibodies.

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Ann Natl Med Sci (India), 15, 1, January-March 1979

In Memoriam

Major General L.K. Ananthanarayanan, AVSM (Retd.),
M.B.B.S., M.S., Ph.D., F.R.C.S., F.A.C.S., F.I.C.S.. F.A.M.S., F.A.Sc., F.I.S.I., and Emeritus Fellow S.I.C.O.T.

Maj. General L.K. Ananthanarayanan, Medical Superintendent and Emeritus Professor of Surgery, University S.S. Hospital and Institute of Medical Sciences, Banaras Hindu University, Varanasi and a Fellow of the Academy, expired on Nov. 6, 1978, due to sudden extensive and repeated Myocardial Infarction.

Born on Dec. 17, 1916, Maj. Genl. Ananthanaryanan, obtained the M.B.B.S. degree in 1940 from Madras. He had his postgraduate training at Govt. General Hospital, Madras (1940-41 and 1949-51); C.M.C. Vellore (1952); Military Hospital, Poona (1950); Royal College of Surgeons of England and Guy Hospital, London (1954); St. Bartholomews Hospital, London and St. James Hospital, London (1955); Royal Infirmary, Edinburgh, Western Infirmary, Glassgow West End Krankenhans, Berlin and University of Vienna (1956).

He started his career as R.M.O. Coy. Commander 2 i/c Field Ambulance and in Mobile Surgical Unit in 1941 in Assam and Burma. In 1945 he was appointed Officer Commanding No.1 Light Fd Amb. at Ranchi. He joined Army H.Q., New Delhi in 1946 as DADMS. From 1949 to 1951 he served as GDMO Surgeon at Military Hospital, St. Thomas Mount, Madras. From 1951 to 1954 he was Surgical Specialist at Military Hospitals, Poona and Secunderabad.

In 1954, he went abroad for postgraduate studies and came back in 1956.

He joined Armed Forces Medical College, Poona in 1960 as Senior Adviser in Prosthetics & Assoc. Professor of Operative Surgery and Commandant Artificial Centre. He became Prof. of Surgery and Head of the Dept. of Surgery in 1966.

He was Examiner for M.S. (Orthopaedic Surgery and Genl. Surgery) at various Universities.

He was Member of the International Society for Rehabilitation of the Disabled, International Rehabilitation Medical Association and Internal Editorial Board of the International Journal of Prosthetics, Orthotics and allied subjects.

He was elected Fellow of the National Academy of Medical Sciences (India) in 1973.

He was author of 'The Krukenbeng Operation', 'Prosthetics Research', 'The Syme Amputation' and co-author of the book entitled 'Fuller Life' published by Ministry of Education. Besides, he had contributed many research papers to various journals in India and abroad.

Maj. Genl. Ananthanarayanan was mentioned in Despatches for gallant and distinguished services in the field. He was awarded the Kartrak Oration Gold Medal in 1969 and Basanti Devi Amir Chand Award for 1971. He was admitted an Hon. Fellow of the F.P.H. in 1963 in recognition of his experience and service in the field of Rehabilitation. He was admitted an Hon. Fellows of the Society of Limb Fitting Experts of Great Britain in 1964.

Almost till the very last he was actively moving about, involved in his multifarious and busy professional duties as Medical Superintendent and Emeritus Prof. of Surgery at University S.S. Hospital and Institute of Medical Sciences, B.H.U., Varanasi. He was cremated with full military honours on the bank of the Ganges on Nov. 8, 1978.

May his soul rest in peace.

Ann Natl Acad Med Sci (India), 15, 1, January—March 1979

Academy Oration–1977

Medical Education in Developing Countries*

B. K. Anand**

Received for publication, June 21, 1978.

I am beholden to the National Academy of Medical Sciences, for inviting me to deliver this year's (1977) Academy Oration, on the subject of "Medical Education in Developing Countries", for which I am most grateful to this august body. I am also thankful to you, Mr. Director, to hold this function at this Institute (R.M.R.I.M.S., Patna), and to you, Mr. President, for kindly agreeing to chair it.

This topic has been of great interest to me, not only during my long career as a teacher, but especially during my tenure as the Vice-Dean and the Dean of A.I.I.M.S., New Delhi, which has been assigned the important role of experimentation with medical education suitable for our country, and later on experience gained by me from the countries of South East Asia, through the office of the World Health Organization. It is thus but natural, that the views expressed by me in this paper, are not only mine; these also reflect to varying extent the concept being developed in the Institution, and the viewpoints expressed on behalf of the World Health body. You may, therefore, excuse me, if you find quotations in this which are drawn from the expressed opinions of some of the authorities of these institutions.

The problems of medical education facing our country, and the other developing countries of our Region, are practically similar. We find that all of them have, by and large, practically patterned their medical education, by copying it from the developed countries of the West, with minor changes and modifications carried out in an ad-hoc manner. It is therefore, realised by all of us, that a time has come when we have to bring about some radical changes in medical education, and adapt it to suit the special needs and requirements of our countries and nations.

Adopted from Western countries, delivery of health care in most countries of our Region so far has mainly depended upon graduate doctors, and manpower development for health services concentrated on the training of traditional categories

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*Academy Oration delivered at the Annual Meeting of the National Academy of Medical Sciences (India) at Patna in January, 1978; and at All India Institute of Medical Sciences, New Delhi in April 1978.

**Emeritus Professor, All India Institute of Medical Sciences, New Delhi.

of medical doctors. Although, since attaining independence in most of the developing countries of this Region, and especially in India, the ratio of doctors to population has greatly improved with a marked increase in the number of medical colleges; inspite of this rapid progress in health manpower production, sophisticated health care has been mostly available to about 20 per cent population living in the urban and semi-urban areas, to the exclusion of the large sections of the community. living in the rural areas, which are by and large depending for health care, besides the sparsely spread health services, on locally available indigenous health workers and traditional healers. This experience of last two to three decades, that inspite of massive investments in medical education, in building health institutions, and the tremendous strides in medical technology, the health of the rural populations has improved very little, has led to the realization by all the countries that there is need for training of health manpower in sufficient numbers, with proper knowledge, skills and attitudes, for providing health services that are adequate and appropriate to the needs of the largest possible segment of the community.

It has further been realised, that the training of more hospital and diseases-oriented physicians and nurses only, is not likely to solve our health problems, in the forseeable future; and thus a new emphasis on the training and utilization of auxiliary and community health workers and their supervisors, for providing at least a minimum of health care to the maximum number of population. In this connection Dr Halfdan Mahler, the Director-General of WHO, has recently stated that, "since it is unlikely that many of the less developed countries can dream of having enough of the traditional health types of personnel, it seems essential that unorthodox solutions be sought. The training and use of health auxiliaries, traditional midwives and healers, may seem very disagreeable to some policy makers, but if the solution is the right one to help people, I think WHO should take courage to tell the member States, that this is the best policy in the long run".

Further, the age-old concept that the medical man is there to care for a patient when approached is no longer relevant to the problems facing the world today. It is the moral duty of medical men to ensure that medical care is made available to the entire population and we promote the concept of health, not as an absence of disease, but as a state of complete physical, mental and social well being. A number of factors militate against the accomplishment of this task—an important one being the inadequate recognition of the role of health in the socio-economic development and the consequent low priority accorded to it by economic planners. However, the outmoded system of medical education far removed from the realities obtaining in developing countries; the brain-drain of alarming proportions; and the unwillingness of physicians to move into rural areas, are also responsible for such a state of affairs.

The burning question challenging the medical profession today is, how to do away with the disparities in levels of health between different groups in the country, and between one family and another. The indifference of health professionals themselves, to some extent, is one of the causes of underutilization, or improper utilization, of the available health resources and manpower.

The general picture in the world today, and this is true of many developing countries, is of an incredibly expensive health industry, catering not for the promotion of health, but for the unlimited application of the disease technology to an affluent section of society. In the present day set-up, with the vast deployment of resources to cope with technology-intensive disease problems, the prevention of disease and promotion of health definitely take second place. To quote an example, in one developing county, which constitutionally declares health a universal human right, 80 per cent of the health budget in one province goes to support one teaching hospital. Such examples are not exceptions, and reflect the obsessional concern of the profession for marginal diseases, which does not perceive the very concept of health.

Man's health is an asset to himself and to his community, and has come to be regarded as a pre-requisite to social and economic development. Promotion of health involves much more than the development of health services; it is dependent, in large measure, on other social and economic programmes, such as rural and urban development, increased production of food through improvement of irrigation and agricultural systems, equitable distribution of food and wealth, improved general education, and a pragmatic demographic policy.

This logically leads to the concept of planning for Health Services and Health Man-power Development. Previously, we used to plan and train health manpower, and then try to fit it to fulfil their roles in the delivery of health care, and thus the health services development has gone on apace from the health manpower development. Although in such a health system, the health manpower consumed the major part of national budgets, yet, in addition to a relative dearth of health workers, we have the anamoly that even those health workers who are available, are not utilized in an efficient manner. This brings into focus the urgent need to define the functions and tasks to be performed, and the types of personnel and quantities of manpower needed.

Such an effort calls for the close coordination of two major components of the health system, i.e., the health care delivery component, and the health manpower component. Unfortunately, such a coordination has been lacking, resulting in the fragmented approach mentioned above. Even within the health manpower component of the health system, there are existing gaps between the main elements of health manpower planning, production of health manpower, and the administration and management of health manpower. Quite often, each of these have proceeded independently with little regard for the other and the whole process for the development of the health services for which it is supposed to cater. The results, therefore, have been deterimental to the consumers, i.e., health services. There has been a recent stress on the concept of integrated health services and manpower development, involving coordination and integration among health manpower development and health care delivery process, tailored to the country's specific situation. This concept means that, in addition to proper planning for the development of health manpower suitable to carry out these functions, we should also have a continuous surveillance and feedback from the health services, for reorientation of the educational programmes on a continuous basis.

Medical education in India and the other developing countries of this Region has been tradition-bound and still pursues a so-called international 'standard'. Consequently, it has become a carbon copy of that in the western countries, instead of being relevant to the health needs of these countries. Here I again quote from Dr. Mahler, the Director-General of WHO, "the traditional approaches to health manpower development in many developing countries, are, perhaps, amongst the most painful of inheritances from the colonial era. The attempts to impose patterns of education, derived from other cultures and former times, have already been proven to be totally inappropriate".

Objectives of medical education anywhere are to produce good 'basic doctors' according to the local needs of the community and the nation. As the national requirements are somewhat different in the developed and the developing countries, the latter have to develop their own objectives for the training of future doctors. An inter-regional conference of WHO on medical education suggested, that the objectives of medical education in the developing countries should be that every doctor should be familiar with all aspects, preventive and curative, of the prevalent health problems of his country, and that he should be competent to contribute effectively to their solution. A 'basic doctor' has also been defined to be one, who is well conversant with the day-to-day health problems of the rural and urban communities, and who is able to play an effective role in the curative and preventive aspects of the regional and the national health problems. A large measure of failure in our countries to provide health services to the majority of the population, is attributable to the type of education that has been provided for health personnel, who are continued to be trained in the traditional way and used in the old pattern, with the result that tackling the health needs of the people in the foreseeable future has become well nigh impossible.

Traditionally, medicine has dealt with treatment of the ill persons. Therefore, teaching of medicine was mainly based on individual patient care, and the province of medicine was considered to be only sickness. There has been a vast professional establishment concentrating on the complicated problems of the few, and so the professional education and training has been geared to a similar performance. Often medical education seems to be patterned to give professional satisfaction to the teachers, rather than education and training to their students. There is, therefore, a crying need to reorganise our system of medical education, and adapt it to meet our own requirements.

Today's medicine deals with comprehensive health care, and its province is man in his entire environment. According to the new integrated philosophy of health, there are three very clear aspects of health : there is the promotive and preventive aspect; there is the curative aspect; and there is the rehabilitative aspect; and it is no longer considered to be coterminus with curative aspect only. The physician of today has not only to provide comprehensive health care to sick individuals in the community, including treatment of acute illness in the hospital, or prevention of recurrence of the disease; he also has to be responsible for the promotion of health in the community, achieved by identification of vulnerable groups, early detection of disease or dysfunction, adoption of preventive measures and remedial actions, and provision of mass surveillance and health education. He also has to organize public health measures directed to the entire community, including environmental sanitation, public health engineering, mass immunization programmes, etc. It is, therefore, essential that the present-day training of physicians, besides including the scientific basis of medicine, has to be further adapted to the local health problems, and by the social, cultural and economic setting in the country. He has to be adept in social anthropology, which will enable him to handle the social proplems of the community. Medicine today does not merely conceptualize "sickness of organs"; it deals as well with wider concepts, such as cultural determinants of health and sickness, social actions for health promotion, community medicine, group behaviour, and other socio-medical issues. Medicine of today, therefore, has to be considered as a 'Social Science' in the broad sense of the word — rather than just a science of curative medicine.

Everyone seems to be in agreement that medical education has to be dynamic, if it has to adapt itself, not only to the new discoveries being made in scientific and technical fields, but also to constant social evolution. On the other hand, it is often difficult to define our objectives of medical education which should conform to the future pattern of social evolution, as we are aiming at a moving target. The present-day students of medicine have to serve the local communities in the next few decades, and they have to perform taking into account the circumstances under which they will work. The development of a health plan for a country demands projection of trained manpower into the furure. As it is often difficult to project the future pattern of evolution of the country's social structure, it is equally difficult to define our objectives of training of medical students, keeping these objectives in view. Although it may be difficult to clearly define our objectives, once we have defined them and prescribed priorities for changes needed in medical educational system, the real difficulty starts when we attempt to implement these resolutions.

A Planning Committee set up by the Royal College of Physicians of London, while discussing medical education in U.K., has written, "Quite apart from the lack of character and ability that may be avoided by improved recruitment in selection, the average medical graduate has defects which are to be attributed chiefly to the manner of his training. He tends to lack curiousity and initiative; powers of absorption are relatively undeveloped; his ability to arrange and interpret facts is poor; he lacks precision in the use of words. In short, his training, however satisfactory, it may have been in the technical sense, has been unsatisfactory as an education." The situation concerning undergraduate medical education in the developing countries of our Region is even worse. Not only have we failed to provide them with a 'satisfactory education', but we have also copied training patterns from the Western countries, without much attempt in reorienting or adapting them to the local requirements. These developing countries have imported technology from the West without adapting it to their requirements.

Of all the roles which a doctor has to play, the one requiring most emphasis at the present time is that of community medicine. In addition to learning about the diagnosis and cure of a community, he should be competent to carry out community health services.

A community consists of persons, families and larger groups with a certain age and sex structure. Health is everybody's business ; the individual, the family, the community, the nation and the family of nations. If ever there were a case for participatory democracy, it would be in the field of health. The family is an essential element in the functioning of society, and in return it is entitled to expect that society provides it with access to progress in the field of health. The doctor's attitude has to be that of a trusted family counsellor, caring for his patients with devotion even when his powers to influence the course of illness are limited.

The physician must cease to be an isolated dispenser of more or less effective medicines and become a socially dedicated person with responsibility for promoting the health of all. In such a situation the traditional approach of teaching of medicine based on individual patient care and mostly in the hospital setting, rather than on community health and local disease problems, is not considered adequate for the training of medical men. They have, therefore, to be trained in a community environment, both urban as well as rural. Thus, for the training of a medical student, there has to be a 'teaching community' comprising a fairly good cross-section of the community, in addition to having a 'teaching hospital'. We have to draw a distinction between the requirements of practice of bedside medicine, as opposed to community-side medicine. Practice of community-side medicine requires that the community as a whole is considered as a patient, and the training of physicians oriented towards that.

Here I quote from Dr. Carl Taylor, who while emphasising medical students field training in community setting, stated, "I am convinced that it is wrong to train young doctors for sophisticated hospital practice and then throw them into a primary health centre in the traditional manner of teaching a puppy how to swim. The excuse has been given that, if students learn the best way of doing things, they will later be able to make appropriate adaptations. This principle may be true when the gap between the teaching situation and eventual reality is not large. It breaks down completely when the gap is as wide as that between a teaching hospital and a rural or urban health centre. It is wrong, morally and educationally, to subject a young doctor to the trauma of trying to make this adjustment on his own. The problems of learning how to live and work in villages, or urban slums, are so difficult and important, that we need our best minds to work them out. and it is the professors who should be in the vanguard of efforts to improve the health of the poor."

In recent years, in some of our developing countries, some curricular reforms have been introduced in medical schools, for reorienting the students learning of medicine in the community in its social and physical environments. Although this concept has been generally accepted, there have been only half-hearted attempts made to actually achieve this objective. The teaching of medicine in most of the medical institutions, is still heavily loaded towards the study of disease and individual patient care, mainly within the confines of the hospital. The only serious attempt which is made to expose the medical students to the social framework of the community, is done mostly in the final phase of internship period, and very little during the undergraduate course. This postponement of the exposure of the medical student to the practice of medicine in the community environment, inclusive of its social, cultural and economic settings, does not seem to be achieving the desired results, as possibly the students' earlier formal training, mainly in the sophisticated environment of the hospital and its laboratories, results in crystalizing in them a mental attitude, which probably makes them suitable for practice only in big urban hospital centres. A serious consideration has, therefore, to be given to change the educational system, so that the training of medical students right from the earlier stages can be undertaken in the community environment.

Realising the importance of training the medical students in preventive and social aspects of medicine, in addition to the curative medicine, during the last two or three decades in our country Departments of Preventive and Social Medicine have been organized and set up in most of the medical institutions. Inspite of this, the products of the present day training programmes are both unwilling, and possibly incapable, of running effective health services in the rural and semi-urban communities. We have, therefore, to reorganize the present system of training in Preventive and Social Medicine, which should not only permeate through the entire course of study, but its practical training has to be incorporated with the clinical training activities, in the hospitals, in the out-patient departments, as well as in the urban and rural community health centres. Such a training in community setting has not only to be the responsibility of the Faculty of Preventive and Social Medicine, but has to be shared by the Faculties of General Medicine, General Surgery, Paediatrics, Obstetrics and Gynaecology, Psychiatry, and some other clinical specialities. We may even consider whether we should not have departments of "Community Medicine", rather than those of Preventive and Social Medicine, as Community Medicine connotes much more than Preventive and Social Medicine.

The doctors needed in the developing countries have also to be adept in being able to manage the various health and disease problems of the communities to the best advantage, within the limited financial resources. It is important to realize in this connection that the major diseases threatening life and destroying efficiency and energy in the developing countries can be diagnosed and treated by using the diagnostic acumen learnt from a good physician, with the help of few simple gadgets, like a stethoscope, a sphygmomanometer, an opthalmoscope, an auroscope, a tuning fork, a patella hammer, a microscope, and some other simple laboratory techniques. The vast majority of common ailments can be diagnosed using these basic skills and instruments. This is rapidly being lost sight of. This is not to belittle advanced medicine, biochemistry, clinical chemistry, microbiology, etc.—all of which are of first rate importance, but it should be stressed that the relative importance of simple procedures should be taught, and that our doctors should not feel that they are powerless without such techniques. To quote an example, a Consultant Physician once visiting a medical college in a developing country, regarded the lack of advanced diagnostic facilities, as a challenge to his skills, and stated that his diagnosis would have been more accurate in only 5 per cent of cases in hospitals had he had better facilities. Dr. Candau, the former Director-General of WHO, while discussing health services in the developing countries, stated, "When one thinks of the enormous efforts that the newly independent countries have made to liberate themselves, it is perhaps surprising that they have not realised that they need to free themselves from what might be called a technical colonialism as well. Technology may be international in substance, but its method of application must be adapted to the situation in which it is to be applied."

Another important factor for creating a frame of mind suitable to the practice of community medicine, is indeed the attitude of medical teachers towards this concept. The influence of senior clinical teachers on the students is profound and if senior clinicians have an adverse attitude towards community medicine, then students will naturally follow their lead to the detriment of the cause. The involvement of the clinical faculty, in the training of medical students in community medicine in the community setting, is essential to achieve the desired training.

The existing situation in the developing countries requires that priority should be given to produce better doctors for the future, more suited to the needs of the communities; or may be, another 'type' of doctor than the kind now being produced without regard to the changing needs of the society for medical care. Some interesting experiments are planned to be undertaken in some of the countries of this Region for the training of such a category of doctors. The Institute of Medicine of Nepal is planning to undertake the production of "community physicians", whose training will consist of 3½ years; and following initial training in basic medical sciences at the Institute of Medicine in Kathmandu, they will be provided clinical and community medicine training mostly in the regional hospitals and health centres. The entry to the course will be open to "health assistants" whose performance at the health centres has been good. It is hoped that such "community physicians" will be more suited, for providing health care in the special situations of rural Nepal. Incidentally, such doctors are also not likely to migrate outside the country. Similarly, in Thailand, it is being proposed to undertake training of "experimental physicians" who may be given basic training for a period of 3 years. The entry to the course being restricted to graduates in science, will enable some of these "experimental physicians" to obtain graduate degree in medicine at a later date, through specially organized courses for the same. It is hoped that the success of such new experiments may set the pace for the future development of another category of doctors required for the basic needs of health care in the rural areas.

Although the great need of our developing countries is for producing mostly 'basic doctors', the fact that some of these doctors have to fill up the roles of future teachers, research workers, and health administrators should not be lost sight of. The rapid expansion of medical colleges has created heavy demands for medical teachers. Further, development of research activities, specially in those fields which are of great relevance to our countries, also requires development of postgraduate and other specialist training programmes. The requirements of such teachers and specialists are relatively small, as compared with the large number of basic doctors required for general health services. Previously, majority of them were being trained in the Western countries. Although the development of postgraduate training centres for training teachers and other specialists has not kept pace with the rapid expansion in the field of undergraduate medical education in our countries, recent trends are for gradually attaining self sufficiency in these training programmes. Such a development will not only improve the quality and quantity of medical education and of health services, it will also be more economical as majority of the teachers and specialists required will be trained within the country or the Region.

Our developing countries have, however, to very carefully determine the areas or disciplines for which such training centres should be developed, keeping in view their requirements, and the existing financial, physical and trained manpower limitations. While most institutions may attempt to develop regional self-sufficiency in training programmes for some of general specialities, such as medicine, surgery, paediatrics, obstetrics and gynaecology, and basic medical sciences, etc., we may only aim to attain national self-sufficiency in training programmes for highly sophisticated super or sub-specialities, depending upon the availability of special facilities in certain institutions or centres. For achieving these targets, it may be better to identify some of the good departments or centres of proficiency, or those which have a potential for such development, and help to develop postgraduate training programmes round these, rather than attempting to initiate such training programmes in all the existing institutions.

The development of postgraduate training programmes will also help in further developing and intensification of biomedical research in our countries, as besides money and institutional resources, conduct of research to a great deal depends upon the availability of trained manpower The research programmes in our developing countries have to be designed with the sole purpose of bringing about a radical change in the approach to provide health care according to the needs of the people, and new and easily applied scientific information and technology has to be developed to achieve these objectives. Research has to aim at finding solutions to our urgent health problems which are within our means. As some of our research requirements are different than the research activities being followed in the developed countries, where the main thrust has been towards the disease oriented establishments, it is important to develop training facilities within our countries for training the specialists and other research workers. For the planning, implementation and analysis of health research, specially in the operational field, multidisciplinary teams are required consisting not only of the professional research workers, but also statisticians, demographers, systems analysts, social scientists, and other auxiliaries, etc.

For proper development of medical education a great deal depends upon the teachers. The teachers in health institutions must, therefore, be experienced, not only in the subjects they teach, but also in the entire methods of teaching. They have to be trained in various aspects of educational sciences, including pedagogy, and preparation of teaching/learning materials. The teachers should also be sensitive and responsible to the ural health problems and needs. They should have orientation in the organisation of health services, operational research, evaluation of services, and the basic principles of health planning, to enable them to plough back this knowledge into their general teaching.

World health Organisation has been concerned, not only about what is taught, but how it is taught, and the evaluation of what has been learnt. Besides holding a number of teacher training courses, it has also helped in the establishment of two Regional Teacher Training Centres in Thailand and Sri Lanka, and further assistance is being provided for the establishment of National Teacher Training Centres in other countries of the Region. One such Centre is being established in Pondicherry in our country. Such centres should be able to provide the resources for teacher training, advisory services, technical support, and operational research, and for effective utilisation of modern advances in pedagogy and educational technology, and their adaptation to local situations.

The world today differs in many respects from what it was 50 years ago. The outstanding difference is change, specially the rate of change. With the scientific and technological revolution going on, a doctor who completed his education 25 years ago, and has learnt nothing since then, is a public menace. A major defect of medical education in the past arose from the erroneous belief that education ceased when the student had completed his University degree. It has now been realized that this was untrue and indeed dangerous. It is no longer possible for anyone to obtain a comprehensive medical training during his years in medical school. Graduation has become neither the end of medical education, nor the beginning of the end, but rather the end of the beginning. In medical education, as in other kinds of education, what matters most is not the knowledge imparted to a man, but what the man himself becomes in the course of acquiring the knowledge. It is essential for every member of the health team, and much more so for the doctors, to be continuously educated with the modern and rapidly advancing standards of acceptable principles and practices. Every doctor has to constantly keep in touch with advances in medicine in the broader sense. Changes are occuring in great rapidity, and he must adapt to the changing conditions of disease pattern, to new skills of diagnosis, to new therapy, and new methods of prevention.

Postgraduate and continuing education are particularly relevant to our countries. The few centres of postgraduate education are geared to the immediate studies required by graduates for specialization in various disciplines. More of such centres are needed, not just to turn out more and more specialist persons, but to give medical men and women an opportunity to refresh their knowledge. Refresher courses for general practitioners in the latest advances in medicine, surgery, psychiatry, community care, and other similar subjects, have to be arranged. Such courses would permit discussion, and give our doctors and health manpower the feeling of the knowledge, that learning never ends, and that they are all part of a rapidly advancing dynamic profession.

Friends, in this talk I have only tried to sum up some of the objectives of medical education in developing countries, including ours. As I have stated earlier, it is not only difficult to clearly define our objectives of medical education; the real difficulty starts when we attempt to implement these resolutions. Still I hope, that this talk may help to stimulate you, to gradually evolve a pattern of medical education, adapted to suit the special requirements of our country. God bless you in the fulfilment of these efforts.

Thank you.

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Achanta Lakshmipathi Oration 1977

Present Status of Management of Disorders of Stress*

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It gives me great pleasure to deliver Dr. Lakshmipathi Oration to-day before this august body of National Academy of Medical Sciences. I am really grateful to our Academy for selecting me to give this oration this year (1977). I hope to present some of the results of our recent studies on the Management of Stress Disorders for the benefit of those interested in this relatively new field.

As you are all aware, Dr. Lakshmipathi was a fully qualified medical man from Madras University. But subsequently he devoted his entire life for the development of Indian medicine. Therefore in this oration dedicated to him, I have selected the topic of management of disorders of stress by using various ancient Indian methods specially the practices of yoga.

Disorders of Stress are nothing but the maladies of modern civilisation. In the Western countries they are the most important causes of mortality and morbidity. Even in our own country, the incidences of these diseases are increasing at a fast rate. What is more alarming is that more and more younger generations are becoming the victim of these diseases all over the world. This is because of the fact that people mostly living in urban areas are becoming more exposed to psychosomatic stress than the people living in less crowded areas in the earlier period. It is known that the most common stress disease—hypertension is hardly everseen in the primitive people of Africa. The pioneer cardiologist of U.S.A. — Paul. D. White stated that when he started working in the beginning of this century at Massachusetts General Hospital, he could rarely see coronary heart disease patients in the wards. But now in the last quarter of this century, these 'Heart Attack' patients are seen in large numbers in the coronary care units of that hospital. All these findings indicate that the incidences of Stress disorders are increasing at a very fast rate, almost in an epidemic form in recent years.

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Amongst all the disorders, hypertension, coronary thrombosis, cerebrovascular accidents, anxiety neurosis, migraine, Thyrotoxicosis, asthma, chronic peptic ulcer, ulcerative colitis, rheumatoid arthritis, diabetes mellitus are some of the important ones. Even amongst them diseases involving cardiovascular system are the most common conditions affecting a large number of people in their productive age. Thus in U.S.A. 50 per cent of the deaths are due to disorders of cardiovascular system numbering about one million people every year. Further it is estimated that 15 to 33 per cent of adult population of that country is having some degree of hypertension. It is known that such a hypertension predisposes the person ultimately to atherosclerosis, heart attacks or cerebrovascular accidents. Since hypertension has an insidious onset, it does not produce any definite sign or symptom in the initial period. In fact many people do not know that they are developing slowly this disease within themselves. They become aware of it only when one of the complications of this disease becomes manifest such as coronary diseases or stroke.

So far we have been mostly blaming various environmental factors for the developments of these diseases such as improper diet, lack of exercise, excessive smoking, family disposition etc. which ultimately predispose the person to develop the disease. The psychologic stress has been given relatively less importance, for the development of Hypertension and other similar diseases. One of the main reasons for such apathy is that it is difficult to measure the quantum of stress in terms of scientific methods nor there was any scope for measuring the response of the person to face such a psychic stress. It is only recently that methods have been evolved to measure the psychic stress as per Rahe's technique and also to measure the response of the person by measuring plasma cortisol and catecholamines in the plasma and urine.

Because of the lack of any such methods of measurement till recently the Physicians use to treat various manifestations of stress diseases by tranquillisers and other related drugs without going to the psychological aspects of diseases. On the other hand psychiatrists mostly looked to these patients only from the psychological angle without going into the details leading to physiological disturbances in these cases. All these fragmentations of patient care in such cases resulted into unsatisfactory outcome. Therefore there is an urgent need for grouping all these cases as psychosomatic or stress disorder for proper evaluation and treatment by using all the medical and non-medical measures.

Etiological factors

In order to consider various etiological factors we would broadly discuss the matter in two groups—(a) Genetic and (b) Environmental.

(a) Genetic factors : There had been much discussions as to whether and how much genetic factors play their role in making a person susceptible to get a particular disease. It had been observed clinically that certain stress diseases like hypertension or diabetes mellitus are seen in many members of the same family. So far, no definite scientific explanation could be given to the reasons why some of these diseases are seen in families. Recently, Axelrod and his associates postulated that possibly they might be having a trait of excessive catecholamine turn-over in their body. Therefore he measured its degrading enzyme MAO in the platelets of patients with schziophrenia. He observed that Platelet MAO was found uniformly low in all these cases which would make them more vulnerable to have excessive and prolonged action of Catecholamine in their brain leading to development of schizophrenia in due course of time.

In view of these earlier findings of Axelrod, we extended these studies for investigating the role of genetic factors in respect of other psychosomatic diseases such as hypertension, diabetes mellitus, peptic ulcer and asthma. We studied the platelet MAO, cholinesterase and histaminase in all these cases and found that in cases of Hypertension there was a reduction of MAO with excess of cholinesterase indicating that they have a greater susceptibility of disturbances of catecholamine Metabolism. Similar was the case with other stress diseases indicating that genetically also the people inherit certain traits of enzymatic deficiencies from their parents which would ultimately predispose them to get certain stress disease if they are exposed to face certain specific types of environmental disturbances.

In addition recently Friedman and Rosenham had classified psychic personalities into two : type A and type B. However no neurohumoral or hormonal studies have been conducted on these people to correlate the type of personalities with biochemical changes in their body. These classifications were made solely on the psychological behaviour of the individuals. A person with type A personality has the trait of excessive drive, too much of ambition and urge to go ahead with material success. However, to achieve all these goals the person will naturally be exposed to excessive stress. Whereas the person with type B personality will make him steady, slow and effective with a definite goal oriented programme. He works for personal satisfaction and therefore will not be much competitive and hence he has less hostility from others. He works steadily and effectively and hence achieves the goal in time without much stress. Though these are the two distinct personalities they cannot be fully relied upon since there can be much overlapping of the two in many circumstances and individuals. Further, as all these factors are based only on subjective findings at the time of interview it may not always be possible to elicit them in patients.

On the other hand, the anthropologists had classified the persons into three categories based on the physical built of the body and psychic behaviour. They classified as — Ectomorph (lean and thin), Mesomorphs (muscular) and Endomorph (heavy). Similarly they had also classified the psychic personality into three— Cerebrotonia, Somatotonia and Viscerotonia. These three types of body and psychic constitutions closely resemble the body and psychic constitutions described in our ancient medicine. They had described **Vata, Pitta** and **Kapha Prakritis,** based mostly on three body humors and **Satwa, Raja** and **Tamas** based on psychological traits. We had carried out certain biochemical studies on these three groups of people and found that the persons with ectomorphic constitution or **Vata Prakriti** has excess turnover of acetylcholine, which also leads to the psychic personality of cerebrotonia or **Satwa Guna.** In persons of second group, mesomorphs **(Pitta Prakriti)** with **Rajo Guna** or somatotonia, one can observe excess turn over of catecholamines. The third group of persons with endomorphic constitution or **Kapha Prakriti** with viscerotonia or **Tamo Guna** have more predominance of histamine in the body. Whenever they are exposed to some stressful situations, any one of these neurohumors become disturbed leading to the development of diseases of respective organs. Thus if there is excess of acetylcholine, they are more likely to develop peptic ulcer, ulcerative colitis or thyrotoxicosis. If there is excess of catecholamines various cardiovascular disorders such as hypertension, atherosclerosis, heart attacks or strokes are more common. If there is excess of histamine they are more likely to develop asthma, eczema, migraine, and other similar diseases. From all these findings one can say that heridity plays an important role in the development of stress disorders.

(b) Environmental factors : Amongst various environmental factors diet, exercise and psychic stress play an important role.

Diet : It is now postulated that a well nourished and a well built body is more likely to get psychological stress whereas a poorly nourished and weak person is more likely to develop various bodily diseases. The well nourished people with excess of fat intake are likely to develop hypercholesteraemia and atherosclerosis. In such cases, if psychic stress is also added to it, they are more likely to develop hypertension and other related diseases very quickly as a result of excess mobilisation of lipids from their depot. Similarly they are also more likely to develop diabetes as a result of disturbance of carbohydrate metabolism. Similarly excess of protein breakdown may lead to arthritis and other similar diseases. Hence dietetic imbalance together with psychic stress can play important role in causing various stress disorders.

Exercise : Lack of physical exercise is another important factor for the development of stress disease. By doing physical exercise one improves the efficiency of microcirculation of the entire body. In such cases if any physical or psychic stress comes they can withstand them much better than others who have not undertaken any such exercise. Apart from physical exercise, the psychic recreation also plays an important role in giving greater confidence in people for facing any stressful situations. Hence from the prophylactic point of view both these things should be properly emphasised. We will discuss this problem once again when we will deal with therapeutic effects of Yoga.

Psychic Stress : The most important cause for the development of Stress disorders is the exposure of a susceptible person to a stressful situation all of a sudden either in a severe form or in the form of mild and yet repetative leading to a chronic stressful situation.

The result will ultimately be the same namely the development of stress disease in due course of time. Formerly it was thought that a specific type of stress such as death of a near relative or sudden loss of finance may give rise to certain specific diseases. But now these views have been changed. Now psychic stress has been measured psychologically depending upon the severity of psychic changes that takes place in a person. Thus Rahe and his colleagues have given scores for each type of stress. Thus death of a wife would get 100 scores whereas loss of money in business would get a score of 50. From these scores one can roughly assess the amount of changes that can take place in a given type of stressful situation. In case of sudden stress the changes are quite quick whereas in chronic cases with repeated exposure to milder stress one develops the disease quite inciduosly.

The chronic stressful situations are many such as moving from rural surroundings to urban areas, getting quick promotions, frequent changes in jobs, strained relationship with wife, poor relation with superiors or subordinates at the place of work etc. All these things seem to have cumulative effect which ultimately lead to stressful situation in life.

Pathogenesis

Whenever a susceptible person is exposed to repeated psychological stress his mental and bodily apparatus undergoes gradual change in order to adapt himself to face the situation. In this process, the most sensitive part of the body namely the cerebral cortex becomes activated first. During this period the person becomes more sensitive restless, irritable and easily exhausted. He passes through the period of insomnia and also looks much worried about the trivial things. If this life situation does not stop and stress continues gradually he goes to the next stage in which predominantly the limbie system and hypothalmus becomes affected. At this stage he becomes emotionally disturbed, he gets more of palpitation and high blood pressure as a result of excess of sympathetic activity. His all other complaints also continue to trouble him. He gets mild tremors, excessive perspiration and loss of weight as a result of excessive mobilisation of lipids.

In the third stage the entire body becomes activated as a result of excess of neuroendocrine activity. There will be increased catecholamines which together with excess of cortisol produces marked catabolic changes in the body along with hypercholesteraemia and increased blood sugar and excess of protein loss. Increased secretion of thyroid gland enhances the metabolic changes of every organ and tissue leading to generalised exhaustion as a result of too much of fight or flight response.

Gradually the patient goes to the fourth stage when the whole body changes becomes localised to one organ or tissue which is susceptible to get the disease as a result of genetic factor and also due to some organic or functional disturbance already present since the early period of life. This is known as "weak organ" condition on which these excessive neurohumoral changes ultimately settle down to cause the organic disease. Thus in people living in endemic goitre region, the thyroid gland is more susceptible for getting thyrotoxicosis. Similarly people eating too much of spicy food are likely to get peptic ulcer. Likewise people living in polluted humid environment are more likely to develop asthma.

It should be realised that when the neurohumoral excess occurs in the body as a result of stressful situations, there will be only functional disturbances in the begining in a given organ. However as the situation continues the disturbance of organic changes appear in due course of time such as ulcer in the stomach or enlargement of the Thyroid gland. Thus when these pathological lesions appear in the X-ray or E.C.G. it is the last stage of the disease and hence they are not reversable. Our attempt therefore should be in the early recognition of these cases and to treat them before irreversible damage occurs in these organs. Then only one can expect to get good and lasting results.

Management : In all these cases the most important thing to remember is that one must take effective preventive measures so that there is no chance of getting any such disease. Although one has no control over the genetic factors, he can certainly influence the environmental factors so that these disorders do not appear at any time in life. Amongst them a good regulated diet and exercise are the most important ones, specially in people of middle age group on whom one should take all possible precautions in this respect. Similarly one must take regular bodily exercises to prevent degenerative changes in various organs and tissues. Amongst all, Yogic Practices which are good both for bodily and psychic health can be of great help for maintaining a good health.

Yoga : Amongst all the methods of yoga, Patanjali's eight methods of Yoga are universally accepted as the best ones. Even amongst these eight methods three are important for a daily practice as a routine for maintaining a good health. They are **Asanas** or postural exercises, **Pranayamas** or breathing exercises and **Dhyana** or meditation. These should be done in a sequential order as per standard techniques preferably after getting a training from a recognised teacher. Normally it takes about 30 minutes — 10 minutes for doing 6 basic **asanas**, 5 minutes for **Pranayama** and the remaining 15 minutes for the meditation. These things will have to be individualised depending upon the physical and psychic make-up of the individuals. Regular practice of these yogic practices always make a person active and energetic both physically and mentally and helps to maintain youthfulness and delays aging process.

Because they improve the microcirculation to all the organs and tissues, the resistance of the body is well maintained through improving the immunological mechanisms. As a result one also develops a type of physical and mental resistance against various stress disorders. This is one of the important reason why these yogic practices have been extensively used all over the western world so as to overcome the ever increasing stress and strain of life and their harmful effects.

Relaxation response and Biofeedback Training : There are many methods in the world which would act almost like yogic practices. Thus relaxation responses, practiced extensively in the west with equally good results. Similarly the biofeedback method in properly selected cases and with necessary facilities this can be a good addition to the Yogic practice especially for meditation. By this one can assess the progress of one's ability to obtain voluntary control over involuntary function. Similarly autogenic training practiced in Germany or Zen meditation popularised in Japan also gives good results. However 3 types of yogic practices should be preferable for a routine use since they are useful both for improving bodily and mental functions.

Therapy of Stress Disorders : It can be well realised that the therapy for stress disorders can be planned depending mainly on the stage at which the patient has sought medical advise.

In the first phase, mainly with psychic features, the principle of treatment would be the efficient delivery of psychotherapy. According to modern trends, such a psychotherapy should ordinarily be given by psychiatrists. However, since the incidence of psychosomatic diseases is high and is increasing daily, it is very essential that every medical man is fully conversant with the principles of psychotherapy. Unconsciously or consciously every doctor does give some or the other type of psychotherapy to relieve tension of his patients. In fact, success or failure of a doctor in the practice of community medicine mainly depend upon how much he depends upon the psychological aspects of medicine to give a complete cure to his patients.

In fact careful listening to the patient's complaints in greater details would itself help the patient to unburden his or her emotional problems. This will relieve the mental tension and cause relief to the patient. Similarly, unburdening of one's tensions to his close relatives or friends everyday seem to be the best first aid to remove mental stress and strain. Hence, these patients with acute mental stress should be encouraged to talk of their mental problems regularly to some one who can analyse their problems and give helpful suggestions.

In addition, in developing countries like India, various other measures are also taken which have a direct bearing on the mind. People usually practice worshiping Gods either at their residence or by visiting a temple. By doing so, they try to unburden their problems and pray the almighty to help them to fulfil their desires or ambitions. Similarly by regular chanting of mantras, reading holy 'Quaran', 'Gita', or 'Bible' loudly may also produce confidence, satisfaction or relief. It looks that many of the traditional practices and ceremonies which are directly or indirectly related to the offerings to God or worshiping God, are nothing but some type of psychotherapy. Inspite of all these prayers and offerings, if one is found to face adverseries of life he faces them boldly and with confidence thinking that they are unavoidable and he is destined to face the situation boldly and win over all these difficulties. Because of such mental make-up and attitudes of life during adverse circumstances he does not get the real impact of stress and strain of life and he faces them with much tolerance and composure, as he feels he has inherited all such adversaries from the misdeeds of his previous life and he can not possibly escape them.

All these psychotherapeutic measures have not only a great preventive value, but also have a great bearing on the curative medicine. However, in the so called civilised communities and well developed nations there is not much scope for such type of psychotherapy. Hence, it becomes apparent that more one becomes civilised, greater are the chances of his developing some type of stress disorder. Therefore, the only way to protect ourselves from the ravages of these stress disorders is to go back to our well documented ancient customs and systems, reform them to suit the modern society and follow them meticulously in order to avoid the development of complications of stress in the later part of the life.

Role of Tranquilisers : One of the most outstanding contribution to the field of psychosomatic medicine in recent years is the discovery of anti-anxiety drugs. At first it was the discovery of Reserpine from the herb, **Rawolfia serpentina,** that initiated the interest. It was found that the use of this drug not only reduced the blood pressure, but also produced a sedative action on the brain. On further investigation it was found that it produced its sedative action mostly by affecting a reduction in the neurohumoral content of the hypothalamus. However, it had many side effects, and hence many synthetic preparations were studied which could stimulate the sedative effects without the side effects. Amongst them maprabromates and diazepams were found to be very useful in such situations. Even amongst the two groups diazepam seems to be having a very specific action on the limbic system and the hypothalamus, by which it selectively reduces neurohumoral content of the diencephalon causing its sedative and tranquilising action. Because of this, it is found to be an effective preparation for overcoming all the stress phenomenon especially during the acute stage. However, one of the drawbacks of this drug is that it may lose its beneficial effect when it is used for long time and it may cause addiction.

In order to avoid these complications, we will have to adopt some alternative measures such as the relaxation exercises, to be discussed later, to give a lasting relief.

Many a time it is very gratifying to observe beneficial effects of these drugs on patients with psychosomatic phenomenon. In fact after the use of these drugs for some period, one can observe a significant improvement in the emotional and behavioural pattern of these patients. They sleep well and their irritability becomes much reduced. Their blood pressure tends to normalise gradually provided there are no other organic changes in the walls of the blood vessels. In addition the use of Beta adrenergic blockers is also found of great value during the acute phase of these disorders.

Now I will briefly discuss the management of different stress disorders, especially with regard to the use of yogic measures in these cases.

Hypertension: This is one of the most common stress disorder that we encounter everyday. It is a wide spread disease through-out the world and its incidence is increasing very rapidly specially in the civilised communities of the western world. Since medical measures alone such as methyl dopa cannot control the disease certain non-medical measures such as Yoga has a great place in the control of the disease. When we studied the neuro-humoral changes, we found that excessive liberation and excretion of catecholamine is the major abnormality in these cases. Hence **Shavasana** which is easy to perform and which had been known to reduce plasma catecholamine, was given to these patients for 30 minutes with gratifying results. Later on they were also given certain other **Asanas** and **Pranayamas** to control their over all mental make-up with excellent results in most of the cases. Many a time the yogic practices were given in combination with drug therapy to provide prompt relief to these patients. In the later stage they were kept only on yogic practices which they were advised to take throughout their life. The urinary excretion studies of adrenaline and noradrenaline indicated that after yogic practice both of them come down to normal level, especially the markedly raised noradrenaline content. From this one can say that yogic practice is one of the best physiological method by which one can control hypertension without administering any chemical agents. Hence it has obviously no harmful effect. Further when chemicals are administered, they always develop some habit forming tendencies which lead to many harmful effects on the body in due course of time. Hence there is an urgent need for popularising yogic practices for these hypertensive cases throughout the world.

Coronary Thrombosis : Since most of the time, coronary thrombosis is an advanced stage of hypertension, its prevention in the early stage of angina by the methods described above would be the best solution. But when the disease has already set in yogic practice cannot do much for them. However a regular practice of **Shavasana** might prevent further deterioration or recurrence of the disease in the immediate near future. Further in our cases, we found that catecholamines were found markedly increased in coronary diseases along with reduction of prostaglandins. Such neurohumoral change was also found in hypertension; but in coronary disease it was found much more pronounced. Therefore there is a definite indication for giving them **Shavasana,** just as we do for hypertension. However our experience in this fields is very limited, since we felt that the disease being a serious one, we should not take the risk of treating these patients with yoga alone. It can at the most act only as an adjuvant to the medical measures to prevent recurrence. It was also found useful in cardiac neurosis cases when seen in early stage.

Chronic Peptic Ulcer : In this disease there is an excess of acetylcholine and histamine content of the blood. Similarly there is marked increase in the plasma cortisol indicating increased stressful state in these cases. However our experience in the well established cases of peptic ulcer with yoga is not of much use though in the early stages with functional gastric disorders, yoga has done much good to relieve their symptoms. In these cases instead, we studied the use of a plant medicine called **Amalaki** in Sanskrit, with gratifying results in a series of carefully selected 68 cases of peptic ulcer. The results of these studies indicated that there occurred a tendency for normalisation of acid secretion with reduction of neurohumoral contents.

Ulcerative colitis : Our studies in ulcerative colitis clearly indicated a marked rise of acetylcholine and histamine in these cases. These changes were found both in mucus colitis — a functional colonic disease and also in ulcerative colitis. In both types of these cases along with standard medical measures we tried the yogic practices with gratifying results especially in the mucus colitis and other functional colonic disorders.

Thyrotoxicosis : This is another stress disorder in which yogic practice greatly help the patients to over come their stressful situations. However we have been always giving the yogic measures along with the standard medical or surgical measures. Thus by adding yogic practice to the known medical measures one can hasten the process of recovery in most of the intractable cases of thyrotoxicosis. In fact yoga can be given in all the different stages in these patients whenever the psychic disturbance is found a dominant factor.

Anxiety Neurosis : This is a very common condition in which the anxiety and psychic disturbances are found clearly from the very beginning. Usually it is found in those persons who worry too much or who do too much of psychic work. They become very nervous, irritable and many a times develop sleeplessness, palpitation **etc**. Their neurohumoral changes indicate an excess of acetylcholine in the blood. In these cases all the three yogic practices produce remarkable good results within a short period of 3 to 6 months. Similarly the raised urinary noradrenaline content comes back to normal within a short period. Further we observed that their subjective symptoms subside much faster than the various physical or biochemical features. Hence a prolonged treatment is needed to relieve their conditions fully. Otherwise the recurrence of symptoms may occur in these cases.

Bronchial Asthma : Bronchial asthma is another condition in which modern medicines have not produced the desired results. Hence we advocated yoga therapy in certain intractable cases with some relief. In these cases most obvious defect is the raised histamine and histaminase content of the blood. At the same time urinary excretion of adrenaline and noradrenaline is reduced and also the cyclic AMP is much reduced. Yogic parctice produced marked change in the neurohumoral contents of urine with raising of catecholamines and corticoid. We postulate that the relief that we get after yoga therapy in these cases might be due to increased endogenous productive catecholamine and cortisol which was abnormally low in these cases.

Diabetes Mellitus : This is another disease in which yoga can help to a considerable extent along with other treatment to control the disease. It has been observed by us that the regular practice of **Asanas** and **pranayamas** reduced the requirement of anti-diabetic drugs. It is more effective in the middle aged persons especially if the diabetes is of recent onset. However these yogic practices will have to be continued throughout their life, failing which the disease may come back again. In many cases it reduces the severity of diabetes by reducing the catecholamine content of the blood which also contributed for the raised blood sugar in these cases. Hence it is useful in all those cases of diabetes which are associated with severe stress and strain of life. In rheumatic disorders of the spine also yogic exercises produce remarkably good results in relatively shorter period of time. In many of these cases drug therapy alone may not do good, especially if it has come as a recurrent disease. In such cases regular yogic practice make the patients happy and free from the disease in relatively much shorter period of time.

Cancer : From our various experimental and clinical observations it appears that psychological stress plays some significant role in development and progress of cancer which is possibly mediated through the release of catecholamines and cortisol from the adrenal medulla and cortex.

It is already well established that cortisol favours the growth of cancer through its immunosuppressive activity. But the catecholamines produce their action mostly through their local vaso-constrictive properties. It is well known that following stress, there occurs excessive release of catecholamines. As the stressful situation continues, one of the susceptible organs or tissues ultimately becomes victim of the disease, because of its weakness due to some genetic factor, or as a consequence of certain environmental factors after birth or in the childhood. If the catecholamines continue to be elevated for a long time, the blood supply to the susceptible organ becomes reduced leading to tissue anoxia. In case the tissue anoxia continues for a longer period in a particular organ, the cells may transform into mutant cells, which can behave abnormally. These abnormal cells in the anaerobic atmosphere can become malignant cells if such a situation continues. It has been also demonstrated by Warburg that the cancerous tissues lack oxygen and these cells grow in anaerobic conditions. From our study we can postulate that chronic tissue anoxia in a given organ induces anaerobic condition which lead to the development of cancer in due course of time. From these studies one can say that psychological stress may cause cancer partly by producing immunosuppression through excessive release of cortisone and also by the excessive action of catecholamines by producing prolonged vasoconstriction and anoxia of the affected organs and tissues of the body. However, it does not appear to be so in cases of sarcoma, where we observed a marked increase in the blood and tissue histamine levels indicating immunological enhancement. These observations tend to suggest that, psychological stress plays an important role in the development and progress of carcinoma in various parts of the body and if this could be controlled by various medical and non-medical measures such as Yoga it would go a long way to give maximum relief to these patients.

In short if one wants to be free from all these stress diseases and also to lead an intellegent, creative life he has to maintain good physical and mental health by the practice of Yoga. Further we can also help all those suffering from various types of stress disorders by way of adding these non-medical Yogic measures as an adjuvant to existing therapeutic regimes, so as to give them maximum relief for a prolonged period. Dr. Laxmipathi after graduating in medicine conducted his vast studies in ancient system of medical sciences to give maximum relief to the people. It is because of this that he attained an honourable position in his life. I am sure if one follows the tradition laid down by him he will be able to do immense service to the humanity specially to those living in our country.

Academy Publications

Liver Cirrhosis—Proceedings of the Symposium held on 5-6 February, 1966 Agra, India. Ed. P.N. Wahi

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Evaluatian of Hypothalmic Pituitary Thyroid Axis and TSH Metabolism after Estrogens

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Effects of daily continuous adminstration of estradiol monobenzoate (E_2B) on TSH levels, TSH metabolism as well as TSH and T_3 responses to TRH were monitored in 5 female rhesus monkeys. Plasma TSH levels in untreated animals ranged from 0.8 to 1.6 uU/ml with mean of 1.14 ± 0.12 SE. A significant increase in TSH levels ($P<0.01$) was observed as early as 48h. following E_2B therapy. Further stepwise and progressive increase over the preceding levels was recorded on day 6,11 and 28 of E_2B therapy. From day 28 onwards the levels plateaued till the duration of E_2B therapy. Ten days after cessation of E_2B, plasma TSH levels came down to the normal range and remained so upto 40 days of observations. Administration of TRH iv (5 ug./kg. bw) consistently increased plasma TSH and T_3 levels in all the animals before and on days 11 and 56 of E_2B therapy. However, in spite of elevated basal TSH and T_3 levels, the magnitude of response monitored as peak maximum rises over the basal level i.e. Δ TSH and Δ T_3 during the 3 tests were not significantly different. Administration of E_2B for 17 days significantly decreased ($P<0.01$) the metabolic clearance (MCR) and increased the extra-pituitary thyrotropin pool (EPTP), but did not significantly alter the rate distribution space (DS), half disappearance time (t 1/2) fractional turnover rate (Kt) and daily production rate (PR) of TSH. However, after 66 days of E_2B these alterations in TSH kinetics were more marked. The t 1/2 and EPTP were significantly increased over the pretreatment as well as the day 17 values. The MCR, Kt and DS decreased signficantly, but daily PR of TSH still remained unaltered. The major alterations in circulating TSH after E_2B therefore appeared to be due to decreased MCR and DS and not due to increased PR.

Introduction

The effects of estrogens on the secretion of pituitary thyrotropin (TSH) are less well understood. The observations of an enhanced TSH response to TSH releasing hormone (TRH) (Mortimer **et al**, 1974 and Ramey **et al**, 1975) and 3 to 5 fold increase in the circulating TSH levels after estrogens (Adams and Maloof, 1970) suggested that estrogens might prime the hypothalamic-pituitary-thyroid axis. However, studies on the effects of estrogens on circulating TSH levels in humans and experimental animals have revealed both stimulatory (Adams and Maloof, 1970) and inhibitory (Fisher and D'Angelo, 1971 and Gross **et al,** 1971) effects on the pituitary thyrotrophs. Unaltered (Rastogi **et al,** 1974) as well increased (Adams and Maloof, 1970 and Weeke and Hansen, 1975) TSH levels and TSH response to TRH have been reported. The question as to where and how estrogens act to influence TSH secretion still remains unresolved. In the present communication we have studied effects of long term administration of estrogens on TSH levels, TSH metabolism and its response to TRH in 5 female rhesus monkeys.

Material and Methods

The studies were carried out on 5 euthyroid menstruating rhesus monkeys (Macaca mulatta) weighing between 4-6 kg. Same animals served as their own controls. Each animal received estradiol monobenzoate (E_2B 50 ug./ kg./ bw/ day) for 110 days. Blood samples 3 to 5 ml. were obtained at regular intervals in heparinized vials by femoral venipuncture before, during and after E_2B therapy. Plasma was separated and stored at -20°C till required for hormone estimations.

To evaluate the pituitary-thyroid axis, TRH stimulation test was performed before and on days 11 and 56 during E_2B therapy. Blood samples were obtained at 0,20,40,90,120 and 180 minutes after iv bolus of TRH (5 ug./ kg. bw). The plasma levels of TSH and tri-iodothyronine (T_3) were assayed in these samples by double antibody radioimmunoassays (Rastogi **et al,** 1973 and Rastogi and Sawhney, 1974). E_2B in oil was purchased from Bengal Immunity Co. Calcutta, India. Purified human TSH (hTSH) and its specific antiserum were obtained as gifts from the Endocrine Study Section, NIH, USA and hTSH standard MRC 68/38 was kindly supplied by the Division of Biological Standards, National Institute of Medical Research, London, U.K. ^{125}I-TSH with a specific activity of 60 to 90 uCi/ug was prepared by the chloramine-T method of Hunter and Greenwood (1962). In preliminary experiments it was ensured that hTSH-RIA was able to satisfactorily detect monkey TSH levels, which when assayed in different dilutions showed parallelism to the standard curve. All the samples from the longitudinal study were analysed in one batch and those from TRH test in another batch to eliminate larger interassay variablity.

To study TSH kinetics, about 0.4 to 0.6 ug of ^{125}I-hTSH in one percent bovine serum albumin (BSA) in saline was injected in the femoral vein and blood samples were obtained at regular intervals for the next three hours. The ^{125}I-TSH content of one ml of plasma was determined by precipitation of the plasma with equal amount of 10 per cent trichloroacetic acid (TCA). The plasma TSH radioactivity as per cent dose administered per litre plasma was plotted on semilog scale against time on ordinary scale. A linear disappearance line was obtained from 20 to 120 min. The t1/2 was determined graphically from the disappearance line. The distribution space (DS) was estimated by extrapolation of the disappearance line to zero time (Odell et al, 1967). The fractional turnover rate (Kt), metabolic clearance rate (MCR) daily production rate (PR) and extra pituitary TSH pool (EPTP) were calculated according to the formula of Gurpide and Mann (1970). The TSH kinetic studies were performed before and on days 17 and 66 of E_2B therapy. The statistical analyses were performed by the analysis of variance.

Results

Figure 1 shows results of TSH kinetics before and on days 17 and 66 E_2B therapy. The t 1/2 and Kt in untreated animals varied between 46 to 76 minutes and 0.91 to 1.5 per cent minute with mean of 59.6 ± 5.5 (SEM) and 1.21 ± 0.29 per cent respectively. Estrogen treatment for 17 days did not alter significantly ($P > 0.05$) the t 1/2 and Kt. However, a significant increase ($P < 0.01$) in t 1/2 to a mean value of 86.4± 4.1 minutes (range (76-100) and significant decrease ($P < 0.01$) in Kt was observed on day 66 of E_2B. The MCR showed a significant decrease ($P < 0.01$) over the basal level on day 17 of E_2B therapy. A significant decrease ($P < 0.01$) in DS was evident on day 66 of E_2B therapy, whereas MCR showed a further decrease. This decrease in MCR and DS was counterbalanced by an increase in the TSH levels and further expansion of EPTP. The mean PR of TSH was 6.1 ± 0.5 mU/day. It did not change in both the studies performed during the course of E_2B treatment.

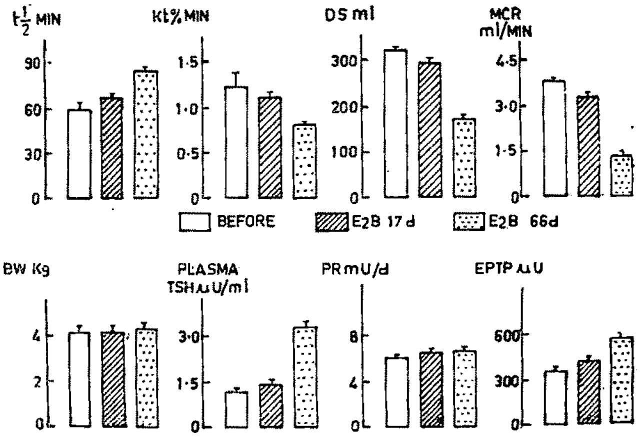

Fig. 1 Showing alteration in TSH kinetics before and on days 17 and 66 of E_2B therapy. See text for abbreviation.

Plasma TSH levels in untreated animals ranged from 0.8 to 1.6 uU/ml. with mean of 1.14 ± 0.12 uU/ml. A significant rise in TSH levels to a mean value of 1.54 ∓ 0.29 uU/ml (0.8 to 2.4) was observed as early as 48h. after E_2B therary. Further significant elevations over preceding TSH levels were observed on days 11, 19 and 28 of E_2B therapy. From day 28 to 110 of E_2B administration the plasma TSH levels plateaued around a mean concentration of 3uU/ml. Ten days after cessation of E_2B therapy, TSH levels were back to the normal pretreatment range and remained so during the 40 days of observation (Fig. 2).

Administration of TRH increased plasma TSH levels consistently in all the animals. Table shows TSH response to TRH before and on days 11 and 56 of E_2B therapy. In spite of a significant rise ($P<0.01$) in basal TSH levels, the overall TSH

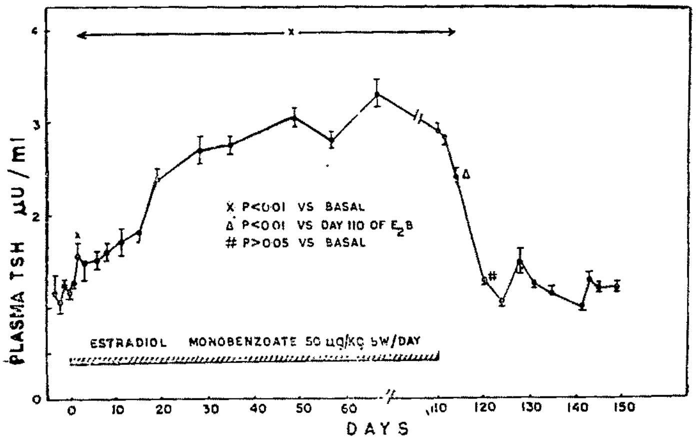

Fig. 2 Showing Plasma TSH levels before, during and after E_2B therapy.

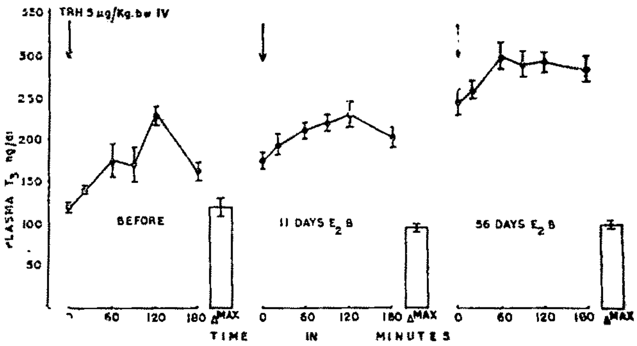

Fig. 3 Mean Plasma T_3 response (±SE) to IV TRH (5 ug/kg bw) before and on days 11 and 56 during E_2B therapy. —T_3 (maximal rise over basal is also shown in the 3 tests.

response as reflected by the sum of plasma TSH level of 20', 40', 60' and 90' as well as the maximum rise over the basal level (ΔTSH) were not significantly altered ($P>0.05$) from the respective pretreatment values.

Figure 3 shows T_3 response to TRH before and on days 11 and 56 of E_2B therapy. Although basal T_3 levels on days 11 and 56 of E_2B were significantly higher than the corresponding pretreatment values, the mean maximal rises over basal (ΔT_3) on both the occasions during E_2B therapy were not significantly altered ($P>0\ 05$) from the pretreatment T_3 value.

Discussion

The observations on the effects of estrogens on TSH levels in human and experimental animals have revealed conflicting results. Both increased, decreased as well as unaltered TSH levels after estrogens have been reported. Some of these disparate conclusions may be attributed to the differences in the estrogenic compounds used, dosage employed, duration of treatment, species studies and the techniques utilized for TSH estimation. To our knowledge this is the first longitudinal study in which plasma TSH was monitored before, during and after E_2B treatment. E_2B was administered in a dose of 50 ug./kg. bw for 110 days to maintain high circulating levels obtained during pregnancy in rhesus monkeys (Hodgen **et al**, 1972).

Adams and Maloof (1970) demonstrated a 3 to 10 fold increase in serum TSH after a single dose of ethinyl estradiol in euthyroid men. The levels reached a peak at 24-36 hours and regressed with a t1/2 similar to that of normal hTSH. Our data confirm this increase in TSH levels as early as 48h. after initiating E_2B therapy.

Table : Showing Mean±SE of TSH response to TRH in 5 female rhesus monkeys before and on days 11 and 56 oF E_2B therapy

	Plasma TSH uU/ml					
	Minutes after TRH					
	0	20	40	60	90	TSH
Before (B)	1.28±0.15 (0.8±1.5)	17.7±3.3 (9.2±30)	17.4±4.7 (8—36)	11.6±2.4 (6—20)	8.1±1.6 (4.8—13)	16.4±3.3 (7.4—28.5)
During E_2B Day 11	2.4±0.15* (1.9—2.8)	18.4±3.8 (8—32)	16.7±5.11 (6.6—38)	11.8±3.7 (6.6—28)	5.9±1.8 (4.2—14)	16.0±3.9 (6.1—29.8)
Day 56	3.2±0.16* (2.6—3.5)	23.3±4 (12—38)	19.1±3.7 (11—34)	16.4±3.3 (9.6—30)	11.9±2.2 (6.8—18)	20.1±4.4 (9—34.5)

*P>0.01

The studies on TSH response to TRH after estrogens have revealed conflicting observations. Both exaggerated (Mortimer et al, 1974 and Ramey et al, 1975) and unaltered (Rastogi et al, 1974) TSH responses to TRH have been reported. Our observations suggested that in spite of a significant increase in basal TSH levels, the magnitude af TSH rise after TRH remained unaltered and estrogens did not significantly after the pituitary secretion of TSH. This hppothesis was further supported by the observation of unaltered daily production rate of TSH after E_2B.

Circulating levels of TSH are the result of its pituitary secretion rate, peripheral metabolism as well as its distribution space. In this study it was assumed that a "steady state" existed during the 3 hour period, the rate of degradation and secretion of TSH remained constant, the radioactive hormone behaved identically to the unlabelled hormone and was rapidly distributed throughout a single compartment. The studies on TSH kinetics 17 days after the initiation of E_2B revealed a definite pattern of decrease in MCR of TSH and increase in EPTP. These alteration in t1/2 MCR, DS, EPTP and Kt were more marked on day 66 of E_2B therapy. Even though there was no alteration in daily production rate of TSH, decreased MCR and DS with normal PR could account for the significantly elevated TSH levels.

How estrogens are able to decrease clearance rate of TSH remains speculative. Experiments with animals have shown that the thyroid gland plays a minor role in the inactivation of TSH (D'Angelo, 1955) and TSH is mainly catabolized in the renal tissue (Cutlelod et al, 1974). As distribution space of TSH was also decreased after E_2B, estrogens could be decreasing the thyroidal and renal uptake of TSH.

Gross et al, (1971) have shown that estrogens in large doses suppressed thyroidal iodine secretion. Because of raised plasma TSH and euthyroid status during normal pregnancy (Rastogi et al, 1974) a relative refractoriness of the thyroid to TSH had been postulated.

The magnitude of increase in serum T_3 levels after TRH induced rise in TSH was not altered by estrogen therapy (Fig. 3) thereby suggesting that thyroidal response to TSH was unaltered by E_2B in the doses utilized. We have also recorded remarkable changes in serum T_3, T_4 and TBG levels in these animals and kinetic data on T_3 and T_4 suggested decrersed metabolism rather than enhanced thyroidal secretion (Sawhney et al, 1978). The major alterations in circulating TSH levels appeared to be due to decreased metabolic clearance and distribution space and not due to increased production rate.

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The Problem of Unauthentic Drugs in India

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The growth of unauthentic drugs is a symptomless disease which poses a threat to individuals, society and government. The unauthentic drugs include substandard, misbranded and adulterated drugs. Detection of unauthenticity is not all too simple. Despite control measures taken by Drug Control Organisations the menace is showing an upward trend. The unauthentic drugs are unsuitable and unsafe for use. A number of factors are involved in the production and sustenance of these drugs. As health of the society is intimately connected to nation's work output and progress it is imminent to institute necessary steps to curtail the menace of the unauthentic drugs. The co-operative effort of the public, pharmacists, physicians, press, politicians, manufacturers and the government is a must to achieve the goal. Some means have been suggested for the same.

Introduction

"The desire to take medicine is the greatest feature which distinguishes man from his fellow creatures"—so said Sir William Osler (1849-1919), a renowned physician, philosopher and medical historian. In our modern society, this desire has reached a notorious stage, creating many problems pertaining to public health, drug-industry and law-enforcement. Of late a serious problem facing the country is the sale of what I would technically call 'unauthentic drugs'. These comprise the popularly known 'substandard' and 'spurious' drugs. Let us first have a general idea of drugs, their production and Government control to maintain the supply of quality drugs. The intimate relationship of production, distribution and consumption of drugs is shown in Fig. 1.

Diseases, Drugs and Society

Modern drugs are sophisticated chemical weapons against diseases. They do not impart new functions to the body organs : they just activate or depress the already existing functions. Almost all of them can produce, depending on the dose and the individuality of the patient, a spectrum of effects extending from beneficial

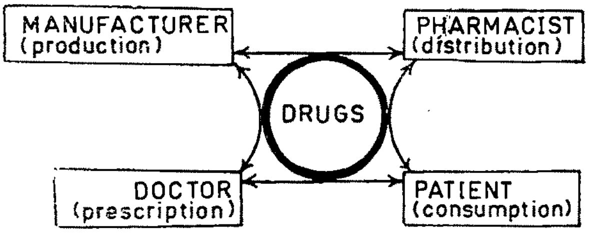

Fig. 1. **Intimate relationship of production, distribution consumption of drugs.**

to toxic. It is indeed astounding to observe how a few milligrams of a drug produces so miraculous an effect in a patient weighing say sixty kilograms. No wonder they have been called 'magic bullets'. At the same time, it is fallacious to consider them as panacea, though they are vaguely considered so by the public. Indeed, this misconceived public faith in drugs is an important factor which sustains the demand and production of unauthentic drugs.

Drug Production in India : Drugs available in India are either imported or manufactured indigenously. The annual production of drugs is worth about Rs. 400 crores. Seventy per cent of the total production is controlled by about 40 foreign pharmaceutical companies. The balance of 30 per cent is shared by about 2,500 indigenous drug manufacturers including 8 per cent public sector. Most of these units are located mainly in Gujarat, Maharastra and West-Bengal.

Drug Control in India : The Drugs and Cosmetics Act was enacted in 1940 and has been in force since 1947. The Act essentially regulates the import, manufacture, distribution and sale of drugs. The Central and State Drugs Control Organisations were created in accordance with this Act. They function under the respective Directorate General of Health Services.

The Central Drugs Control Organisation has the overall control of drugs, including the approval for their import or production of new drugs within India. It also co-ordinates with the State Drugs Control Organisations which are responsible for controlling quality of drugs manufactured, distributed and sold in their areas. Central and State Drugs Control Organisations employ Drug Inspectors and Drug Analysists. It is a herculean task for these organisations, with the paucity of trained personnel and limited drug analysing facilities to check periodically the identity, quality, purity, potency and sterility of the drugs, available in the market.

Unauthentic Drugs (Fig. 2)

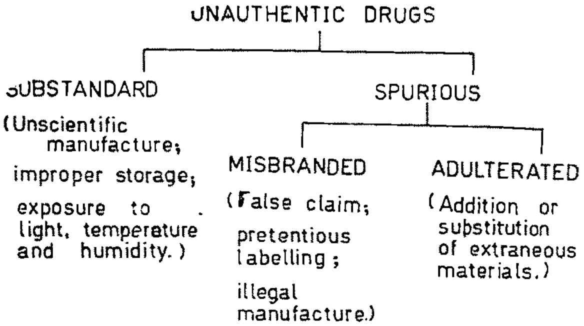
UNAUTHENTIC DRUGS
SUBSTANDARD
(Unscientific manufacture; improper storage; exposure to light, temperature and humidity.)
SPURIOUS
MISBRANDED
(False claim; pretentious labelling; illegal manufacture.)
ADULTERATED
(Addition or substitution of extraneous materials.)

Fig. 2. Classification of unauthentic drugs.

Sub-standard drugs : Sub-standard drugs are those that do not conform to the standards laid down by the Drugs and Cosmetics Act. Most of the instances wherein complaints are made regarding the efficacy of a drug stem from the fact that the amount of the active ingredient contained in the alleged sub-standard preparation is less than what is indicated on the label. This may be due to unscientific manufacturing or packaging, or improper storage

The factors responsible for the deterioration of drugs in relation to storage are humidity, light and temperature. Moisture alone is sufficient in many instances to affect drugs adversely and so also light and temperature. Improper storage will also lead to the growth of microorganisms such as bacteria, fungi, which in turn will spoil the drugs.

Thus it becomes essential to ensure not only the chemical composition of a drug but also the physical conditions under which this is manufactured, stored, packed and dispensed. Reputed firms are not always honest to market standard quality drugs.

Spurious drugs : The popular connotation "spurious drugs" means those drugs which are not genuine, or are false; colloquially they are called "fake" or "bogus" drugs. These drugs are not only ineffective but also harmful. The upsurge of spurious drugs in recent times is due to the clandestine activity of the unscrupulous manufacturers.

The term 'spurious drugs' does not specifically figure in the Drugs and Cosmetics Act, though it is broadly defined under the heading 'misbranded drugs' and 'adulterated drugs'.

Misbranded drugs : Misbranded drugs are those drugs which do not contain the active ingredient they claim to contain or are manufactured and labelled as a product of another manufacturer who is reputed for that product or is produced by a person who does not possess valid licence.

Adulterated drugs : Adulteration is an admixture or substitution of inferior, impure, inert, or cheaper ingredients for gain, deception or concealment.

General public is amply aware of 'watered-milk', 'cowdung mixed pepper', 'saw dust packed cigarette' and the like. And now, there are 'chalk-mixed'-drugs, which are so designed and dressed to mimic the genuine one that neither the doctor nor the patient, nor an analysist can detect its genuineness without analysing the materials.

The common methods employed for adulteration are :

(a) addition of worthless materials like chalk powder, cowdung ash, starch **etc.** ;
(b) Substitution of inferior commercial variants or exhausted drugs or superficially cheaper, natural substances, usually having no relation to the genuine drug ;
(c) manufacture of artificial materials which will simulate the general form and appearance of the drug.

Detection of adulteration involves the establishment of the identity of the adulteration material and the analysis of the quality and quantity of the active ingredient of the drug with the help of various analytical procedures.

Consequences of using the Unauthentic Drugs : The unauthentic drugs when used are either ineffective or sub-effective or prone to produce toxic effects. Sometimes they are lethal. They cause complications to the already existing disease. Sometimes these drugs are more dangerous than the disease itself. In short they are unsuitable and unsafe for use. (Fig. 3)

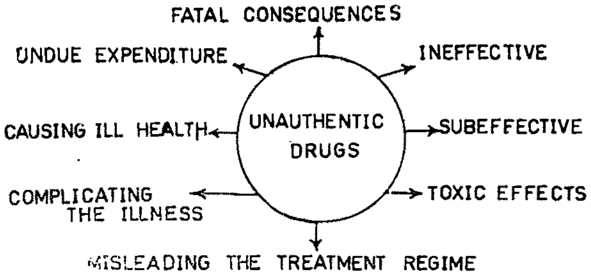

Fig. 3. Consequences of using unauthentic drugs.

More than 30 cases of detection of spurious drugs during the period January to October 1974 have been reported. Out of these, 13 highlighted deaths and the Kanpur Hospiral 'glucose-saline' tragedy gave a stunning blow to the public faith. An underground drug firm in Bombay was unearthed, which sold Tetracycline capsules containing nothing but turmeric powder, the colour of the latter resembles that of the former. In some of the commonly available pain relieving remedies, nothing but chalk powder has been the only ingredient present. Many multivitamin preparations, sulpha drugs, antibiotics have also been found to be unauthentic. Many a 'tonic' which is advertised to give 'vim, vigor, vitality' (and what not) has been detected to contain saccharin with some flavouring agents and non-permitted colouring materials.

The ineffectiveness of a bogus drug, will certainly mislead the physician to conclude the drug as ineffective, or compelling him to substitute another drug which may be more toxic and less effective.

Factors involved in the production and sustenance of the unauthentic drugs :

Manufacturer/Manufacturing process : The active ingredient of a modern drug undergoes a 'make-up' during manufacturing process so as to 'dress' them in convenient and attractive forms such as tablets, capsules etc. For example, a tablet not only contains the active ingredient but also some inert materials to give it a reasonable size and shape to the finished product. These materials include adjuvants, binders and disintegrators, all of which should not interact with the active ingredient. Only scientific selection of these materials will ensure the proper composition of a drug.

Only a few manufacturers strictly adhere to the required manufacturing processes, storage facilities and packaging. It is at this stage that the government should act with utmost care and determination to licence, inspect and regulate the production of genuine drugs. Sampling and analysing the drugs once they have come to the market, is not practicable. Catching the tail leaving the head is obviously of no avail.

Illiteracy : The illiteracy in the country is such that the major population can not read the label or literature of a drug, which is written in English. To add to this difficulty is the confusion created by the marketing of a drug under a number of brand names.

Hospitals : It is shocking that hospitals have become the main victims of receiving adulterated injectible medicines. Generally, the drug supplying firm which has quoted the lowest tender is accepted for supply. In the first instance, the supplier satisfies the hospital authorities with genuine stuffs but later on may substitute adulterated or sub-standard drugs. The hospital authorities have no facility to check the genuineness.

Unscrupulous manufacturers and distributors employ this method to recover the losses incurred in quoting low prices.

Containers of medicaments : The Drug rules do not apply to the manufacturers of containers, closures, bottles tubes, aluminium foils. rubber caps etc. These are most often found to be sub-standard. A poor quality rubber closures of an injectible product may contaminate the solution of the medicine. Inadvertent use of these contaminated products may prove to be fatal.

Storage facilities : Neither the manufacturers nor the distributors nor the retailers have adequate storage facilities, so also the in-transit facilities from one place to other. Improper storage conditions are likely to make a. drug sub-standard which is otherwise genuine.

Retailers : Consumers purchase drugs from retailers who call themselves by various names like 'druggist', 'chemist', 'pharmacist', 'dispensing chemist' **etc. etc.** These retailers by and large do not possess required qualifications. Their main aim is to earn money. The retail shops run by these people are potential sanctuary for the distribution of worthless drugs. General public is very vulnerable to buy drugs without cash-memo to save some money. This facilitates retailers to escape from the clutches of law even if they are caught. It is not uncommon that medical representatives sell the physician's samples and expired medicines to retailers. As retailing is the final common pathway for the dissemination of the drugs, strict surveillance should be exercised on retail store.

Medical practitioners : The ethical medical-practitioners do get bad name due to the inadvertent use of the fake medicinal as it is hardly possible to distinguish from the genuine. Many of the illegal practitioners, practice subtley in rural and semi-urban areas. Behind the curtain they use bogus and substandard drugs to treat their patients thereby injuring the health of the poor people.

Government : Government have taken several legislative measures from time to time to curtail adulteration. But it is observed that the evil instead of being on the decline has been steadily increasing. No matter how stringent the provisions of law may be, it would be of no avail whatsoever unless the Act is properly and effectively administered. In a vast country like India, the existing Government machinery is perhaps absolutely inadequate to keep a proper control on all manufacturing units and the distribution outlets. Drug inspectors have a major role to play. They can perform so, only if they are well trained and adequately paid. Many States do not have analytical laboratories for the testing of drugs. Throughout the country there are about 74,000 dealers and 2,500 licensed manufacturers. But in contrast there are about 200 drug control officials.

Loan licence : Under the current legislation, getting drugs manufactured without having a manufacturing unit or elsewhere away from one's own manufacturing unit or 'loan licence' basis is permissible. This practice gives scope for the production of substandard and adulterated drugs.

Politicians : The spurious drugs manufacturers are sometimes given 'protection' and 'assistance' by unscrupulous politicians, to achieve their own personal gains,

Consumers : A consumer with meagre knowledge about drugs is in a pathetic plight on one hand of being unable to distinguish a good drug from bad one and on the other hand to suffer from the ill-effects of a bad drug with the expenditure of money.

Buying medicines from unauthorised drugs stores, self medication, consulting with unqualified and unregistered practitioners and falling prey to the fanciful advertisements are some of the weak inlets through which the fake and substandard drugs stealthily creep in. The private organisations like the Consumer Council of India have been doing a commendable job to educate and help the public to make them aware some of the problems of drug adulteration.

How to curb this menace

1. The whole affair of control of drug production, distribution, licensing, checking and quality controlling should come under a separate, full fledged and adequately manned Central Directorate with its own subsidiaries in each State so that uniform standards can be maintained throughout the country.

2. Substantial expansion of drug-analysing facilities in each State should be undertaken. Drug-analysing laboratories can be attached to the medical colleges of the country.

3. Periodic inspection of manufacturing firms retail stores, hospital stores etc. should be intesified.

4. A national code should be evolved for easy identification of approved medical stores. The approved medical stores should display a specified sized (say 2 metres x 1 metre) red painted 'name-board', wherein the name of the drug store and the licence number should be written in white paint conspicuously both in English and in the regional language. The consumers should be advised through various publicity media to buy drugs only in these approved shops, with cash-memo. They should be educated that they encounter risk if they buy from any other source. In this way, public can be protected from falling prey to the unauthorized retailers.

5. Consumers should examine the packing, label and containers to make sure that

the seals are intact, that the retail price on the label has not been manipulated, that the date of expiry has not crossed the limit. They should insist for a cash-memo.

6. Spurious drug manufacturers are no doubt responsible for mass murders. They should be treated as murderers and punished accordingly.

7. In recent years, there has been a great increase in the number of misleading and objectionable advertisements for drugs in newspapers, magazines, film theatres **etc. etc.** These advertisements tend to cause the ignorant and unwary to resort to self-medication with harmful drugs or to resort to quacks who indulge in such advertisements. It is necessary in the public interest to put a stop to such undesirable advertisements. In this regard, effective and strict implementation of the Drugs and Magic remedies (Objectionable advertisements) Act, 1954 is greatly warranted.

Acknowledgment

I am very thankful to Prof. N.K. Bhide, Department of Pharmacology, All-India Institute of Medical Sciences, New Delhi; Dr. S. Krishnamoorthy, Secretary, Consumer Council of India, and Dr. Dasgupta, Assistant Drug Controller, Central Drugs Control Organisation for discussions.

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Complications of Anesthesia

"An Emergency Anticipated Ceases to be an Emergency"*

**Quintin J. Gomez

In spite of all the advances made in the last fifty years, morbidity and mortality statistics worldwide show that the administration of safe anesthesia for all cases has not yet been achieved. The scientific progress made has not yet been reflected in the daily work of the operating theatres in many areas of the world. The desire of people not adequately trained in the administration of anesthetics to utilize sophisticated and complicated techniques has resulted in accidents which could have been avoided. Moreover, the accidents which did occur were inadequately managed resulting in fatal outcome in the majority of cases.

It is apparently the 'simple cases' which oftentimes give the most complications because the anesthesiologist approaches the administration of anesthesia with complacency and over-confidence. It is not sufficient to have the patient wake up from anesthesia because the effects of poorly administered anesthesia may manifest themselves weeks or months later. The physiological changes introduced by the various anesthetics may not be discernible immediately without the help of accurate monitoring of various parameters. It is therefore essential that whoever is administering an anesthetic be aware of these subtle physiological or biochemical changes. No two patients react similarly and even the same patient may react differently when given the same anesthetic two or more times. The main fact to remember is that there is no fool proof anesthetic or anesthetic technique; that there is no absolutely safe anesthesia.

A complication is defined medically as "the concurrence of two or more diseases in the same patient". While the administration of anesthesia is not a disease, it is a stress deliberately induced in a patient who already has a disease. This stress, if not compensated for adequately, increases the risk of surgery.

Types of Complications :

A. Predictable Complications : Because these complications can be predicted, they can be prevented.

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* Guest lecture delivered under the auspices of the National Academy of Medical Sciences (India) on September 27, 1978, at the A I.I.M.S., New Delhi.

** President of the World Federation of Societies of Anaesthesiologists.

1. **Complications due to mechanical problems** : Under this group are the complications resulting from defective anesthetic apparatuses such as inaccurate flowmeters, inaccurate vaporizers, malfunctioning breathing valves, improper fittings, cross-contamination, kinking and obstruction of breathing tubes and orotracheal airways, breakage of spinal or epidural needles and catheters, increased deadspace, improperly filled or labelled gas supply tanks.

2. **Complications due to pharmacologic problems** : These are mainly overdosage of anesthetic drugs, drug interaction, use of agents which are contraindicated in certain diseases, use of drugs which have not been fully investigated ("when in doubt don't"), underdosage of anesthetic drugs, drug incompatibility.

3. **Complications due to inexperience** : The inexperienced anesthesiologist must rely on those techniques and agents with which he is most familiar until such time as his experience and knowledge permit him to widen his armamentarium. He should not hesitate to call on the more experienced anesthesiologist for assistance should he find that the problems facing him are beyond his capacity to solve. Safety is the cardinal rule and pride has no place in the practice of Anesthesiology.

4. **Complications due to lack of adequate preparation of the patient** : The induction of anesthesia in any patient is a stress which is deliberately imposed upon that patient and added to the stress of the surgical procedure. Therefore, if we expect the patient to tolerate anesthesia and surgery we must always attempt to prepare that patient to withstand this stress as efficiently as possible. All of the organ systems of the patient that will be involved by the stress of anesthesia and surgery must be brought up to as near normal as possible before operation. The main organ systems concerned are the respiratory system, the cardiovascular system, the hepatic system, the renal system and the central nervous system. The choice of anesthetic will therefore depend on the state of function of these systems.

Equally important is the immediate postanesthetic period which means that period from the termination of surgery until full recovery from the anesthetic occurs. Until all possible effects of the anesthetic no longer present a danger to the postoperative patient, the anesthesiologist's duty has not ended.

5. **Complications due to carelessness** : This is the most inexcusable cause of complications of anesthesia and is due to a failure to appreciate the danger, a failure to observe the patient carefully during the entire intraanesthetic period, a failure to take proper remedial measures soon enough, a failure to prepare the patient properly before anesthesia, a failure to follow the patient into the immediate postanesthetic period.

B. Unpredictable Complications : Because these complications cannot always be predicted, they are not always preventable.

1. Complications due to pharmacologic problems : Drug idiosyncracies, drug interaction, anaphylactic reactions.

In spite of all the knowledge available in pharmacology today, there will undoubtedly occur instances in which a patient will react in an unexpected manner to a given drug. The responsibility of the person utilizing that drug is to stop immediately its administration or if it is a drug which has already been administered via a route which does not permit its withdrawal, then all adequate measures to control the results of this untoward reaction must be instituted with the help of other doctors, if necessary. It is necessary that the anesthesiologist know that patients today are being given numerous drugs which may interact with anesthetic drugs either in their original form or by means of their metabolic by-products. It is the responsibility of the anesthesiologist to widen his knowledge along these lines.

2. Complications due to physiological problems : Respiratory, cardiovascular, hormonal, renal, hepatic, central nervous system pathology.

These organ systems are primarily concerned in the elimination and detoxification of anesthetic drugs. They are also the systems most rapidly affected by anesthesia. Although there are many available tests to determine the adequacy or inadequacy of these organ systems, there will be the occasional patient who will not react in a predictable manner to the various anesthetic agents that are widely used today. Alertness to this possibility and preparedness to handle the situation are the only insurance that the complications will not become fatal.

3. Psychiatric complications : In recent years drugs which have the ability to dissociate the person from his surroundings or to induce amnesia have come into general use. Although in the majority of instances the results obtained with the use of these drugs have been satisfactory, there are nevertheless a number of patients in whom the results have been harmful. It is in this area of medicine where predictability is most difficult.

Summing up : We are still not certain how anesthesia induces unconsciousness and yet are using powerful drugs which can produce unconsciousness in a few seconds. We are literally bringing our patients to the brink of death and pulling them back again.

What a tremendous responsibility this is !

Thank you.

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Academy News

Seminars and Symposia :

Human Reproduction : A seminar on **Human Reproduction** was held at K.E.M. Hospital, Bombay, on Sunday the Feb. 11, 1979 under the joint auspices of the National Academy of Medical Sciences (Maharashtra Chapter) and the Bombay Obstetric & Gynaecological Society.

The seminar was attended by about 300 Gynaecologists, Pediatricians and learned members of the other disciplines. It was a great success.

Nation Drug Policy : The Academy in collaboration with the Indian Council of Medical Research and Indian Pharmacological Society organised a symposium on **National Drug Policy** at the A.I.I.M.S., New Delhi, on Dec. 30, 1978, under the Chairmanship of Dr. R.K. Sanyal, FAMS. The Symposium was a great success.

The proceedings of the symposium will soon be published in a Special Number of the ANNALS of the N.A.M.S.

Chapters :

The **North Chapter** of the Academy held its 18th meeting on Nov, 19, 1978 at the Punjab University Extension Library Auditorium under the Presidentship of Prof. P.N. Chhuttani. The meeting was attended by over 150 doctors including Fellows and Members of the Academy. Sixteen original Scientific Papers were presented which were followed by extensive discussion.

The **Bihar Chapter** of the Academy appointed the following faculty for conducting courses for MNAMS candidates :

Dr. L.S.N. Prasad, FAMS
Dr. B. Mukhopadhayay, FAMS
Dr. A. Sinha, FAMS
Dr. G. Achari, FAMS
Dr. K.P. Sinha, Medical College, Patna
Dr. S.P. Verma, Medical College, Patna.

A meeting of the Fellows and Members of the **Bihar Chapter** was held at Red Cross Bhavan on Jan. 27, 1979 with Dr. L.S.N. Prasad, in Chair. The meeting was also attended by Dr. M. Singh, Principal, Patna Medical College, and Dr. U. Prasad of University of Malaya, Kuala Lumpur, by invitation.

Dr. P.N. Chhuttani, President, addressed the meeting. He appealed to the members to make efforts to raise funds for the Building Fund of the Academy.

The President also referred to the new procedure and requirements of election of President of the Academy.

He also elicited views of the members regarding conferring Hon. Membership (M.A.M.S.) besides these who secure it by examination. It was suggested that Hon. Members be conferred M.A.M.S. and those by examination as M.A.M.S. (N.B.E.).

President's visit to South and Eastern India :

Dr. P.N. Chhuttani, President of the N.A.M.S./N.B.E., toured South and Eastern India from Jan. 19, to Jan. 31, 1979.

The President's one day visit to Madras was packed with engagements. Apart from the Symposium on 'Delivery of Health Care' and the 'Sarabhai Oration' he had discussions with leading physicians present in town.

At Gauhati, he was received by Dr. J. Mahanta, Principal of the Gauhati Medical College. Dr. Chhuttani met the staff individually as well as collectively and was also able to address the Postgraduate students apart from meeting some of the dignitaries of Assam. Dr. Mahanta, as well as his colleagues were all very enthusiastic about the objectives of the Academy as well as the MNAMS examinations. They were appreciative of Gauhati having been given a Centre and were even keen that Part-II exam. should also be held at Gauhati, The President impressed upon them the great need to organise training programmes not only for those who were on their roles as Postgraduates, but also for the peripheral specialists including many who were working in the adjoining hospitals manned by Indian Tea Association, the Assam Government and the Army.

Dr. Mahanta also put forward the suggestion that the Academy might lend a faculty for certain unrepresented specialities when required.

Dr. Chhuttani's visit to Dibrugarh was even more intense and equally fruitful. He was pleased to see how well run Dibrugarh Medical College is considering the disabilities of the peripherally situated State. Dr. N. Zaman requested the President that the Academy should help them in not only making Dibrugarh a Centre for examinations but also provide occasional faculty on loan for selected courses of training. The President promised to give his request full support.

The President also visited the Digboi Hospital run by Assam Oil Company and met specialists working there. They were all keen to participate in the activities of the Academy as well as take up the N.B.E. facilities i.e. MNAMS.

At Calcutta, a meeting was held where 16 Fellows attended. The need for funds for the Academy building was discussed and all promised to collect money from the Industrialists as also from the Government of West Bengal.

At Patna, the President was able to meet almost all the senior Fellows at Rajbhavan. At the formal meeting on 27th January, 1979 the Principals of the two colleges were also present. A suggestion was put forward that the Membership of the Academy should be of two kinds, namely, one awarded by the N.B.E. and the other by the Academy without examination. Dr. L.S.N. Prasad suggested that the Academy should take note of the International year of the Child and work out a fruitful programme for the same.

The Pediatricians of Bihar had assembled for a meeting to consider their contribution to the I.Y.C. The President inaugurated their meeting and addressed the Paediatricians. He was able to put across the objectives of the Academy and there was a general appreciation of what the Academy was trying to do for the cause of Medicine in general and specialists in particular.

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N.B.E. News

Recognition of Pre-1976 MAMS qualification :

A Viva examination will be held on May 4 and 5, 1979 at New Delhi, for Pre-1976 MAMS qualified candidates.

The **Aide Memoire** regarding regularisation of the position of Members who have been awarded M.A.M.S. by examination prior to 1976 is as follows :

The Medical Council of India has recognised, after inspection, the MNAMS degrees awarded by the Academy in case of examinations conducted since 1976 and the same have been included in the First Schedule of Indian Medical Council Act 1956 with the approval of the Govt. of India.

A number of members who had been awarded the membership of the National Academy of Medical Sciences by Examination prior to 1976 raised the question of their status and indicated that the M.A.M.S. (by examination) obtained by them should also be included. The above matter was considered at the meeting of the Executive Committee of the National Board of Examinations held on 15th October, 1977, and the following decision was taken :

> "Item No. 20 : The Executive Committee recommended that a Board of Examiners to conduct a Viva-voce in specialities may be constituted and to send this recommendation to the Medical Council of India for further consideration."

The matter was taken up with the Medical Council of India and the Govt. of India. The MCI has agreed to inspect the examination and Government's approval has been received. The matter was again considered by the Executive Committee of the National Board of Examinations at its meeting held on November 4, 1978, and the following decision was taken :

> "It was agreed that more than one examination may be held as and when necessary.
>
> It was agreed that the MCI representatives be present at the first examination in any of the subjects and once approval is accorded, the subsequent examinations need not be inspected. Suitable guidelines may be given to the examiners regarding the standard expected by the Academy/MCI".

A total of 77 candidates had been successful in the M.A.M.S. examination prior to 1976.

Of the above, candidates whose addresses were available, were informed of the decision taken by the N.B.E. and the approval of the Medical Council of India and the Government of India. Replies from 36 candidates were received. The subjects, with number of candidates in each, is given below :

Subject	Number of candidates
Anatomy	1
Medicine	4
Psychiatry	2
Radio-therapy	1
Anaesthesiology	2
Surgery	8
Ophthalmology	8
Obstt. & Gynae.	4
Orthopaedics	1
Social & Preventive Medicine	5
Total :	36

The Medical Council of India have agreed to inspect the Examination.

The pre-1976 pattern of M.A.M.S. examination included a Primary (Part-I) and Final (Part-II) examination.

Theory and Practical examinations were conducted in both Primary and Final. Candidates were required to pass in theory before being eligible for Practicals.

The examinations were conducted by FELLOWS OF THE ACADEMY who were Senior Teachers of long experience and Inspectors of the Medical Council.

It will be noted that the examination prior to 1976 required candidates to appear for a Practical examination in both the Primary and Final. The existing pattern of MNAMS requires a candidate in case of Primary (Part-I) to pass in Theory only except for subjects in Basic Medical Sciences (Group A).

The standards of the pre-1976 examination was in all respects equivalent to the existing MNAMS examination.

Government approval for inclusion in the 1st Schedule of the M.C.I. Act-1956 has been received for all attached subjects in which the interview is being conducted EXCEPT ANATOMY (in which no candidate has so far appeared for the Final).

In view of the special circumstances in which the above examinations had been arranged, the above aide-memoire is for information of the Inspectors and the Examiners.

Candidates will be informed of the results of the Viva on completion of the interview, and also the approval of the Govt. of India on receipt.

February, 1979 examination

The 7th written MNAMS examination was held on 5th & 6th Feb., 79 at 19 centres including London. The practicals examination was held at 5 centres, The practical examination in certain subjects was held at P.G.I., Chandigarh for the first time. The result of Part-I & Part-II is given in Tables I & II.

Recognition of MNAMS examination

The M.N.A.M.S. examinations in E.N.T., M.C.H., Dermatology & Combined Dermatology & Venereology were inspected by the Inspectors of the M.C.I. in the year 1978. The following qualifications granted by the N.B.E. have been recognised and included in the First Schedule to the Indian Medical Council Act, 1956 :-

M.N.A.M.S. (Otorhinolaryngology)

M.N.A.M.S. (Dermatology & Venereology),

The M.C.I. has also inspected the examination in the following subjects. The reports are awaited.

1) Respiratory Medicine
2) Paediatric Surgery
3) Neuro-surgery
4) Cardio-thoracic Surgery
5) Pathology (Morbid Anatomy)
6) Integrated Maternal Child Health Care.

Nomination of Vice-Presidents

Dr. A.S. Paintal, Dr. M.K. Chhetri and Dr. B. Ramamurthi completed their 3-year term as Vice-Presidents of the N.B.E. The Min. of Health & Family Welfare have nominated the following Vice-Presidents for a period of one year with effect from Feb. 5, 1979 :

Basic Medical Sciences : Dr. K.P. Bhargava vice Dr. A.S. Paintal.

Medicine & Allied Sciences : Dr. L.S.N. Prasad vice Dr. M.K. Chhetri.

Surgery & Allied Sciences : Dr. Atm Prakash vice Dr. B. Ramamurthi.

Community Health : Dr. N. Jungalwalla will continue as Vice-President for Community Health.

Introduction of new subjects : The syllabus for the following subjects have been formulated and approved by the N.B.E. :

a) Forensic Medicine
b) Biochemistny (For medical graduates only)
c) Nuclear Medicine
d) Aviation Medicine

It is hoped to conduct examination in the above subjects from August 1979.

Examinations abroad

Arrangements have been made by kind permission of the Min. of External Affairs for inclusion of information regarding the examinations in the "Information Service India" which is circulated to all Embassies and High Commissions abroad.

Table I. Primary (part-I) MNAMS Examination (February, 1979)

Subjects	No of Candidates appeared	No of Candidates passed	
		Written	Practical
Basic Medical Sciences			
Pathology	4	3 (Five appeared in Practical)	2
Pharmacology	1	1	1
Medicine & Allied Sciences			
Medicine	114	53	—
Pediatrics	38	11	
Psychiatry	24	3+(1 result awaited)	
Radio-Diagnosis	6	2	
Radio-Theraby	4	1	
Dermatology	13	1	
Respiratory Medicine	10	5	
Anaesthesiology	21	7	
Surgery & Allied Sciences			
Surgery	116	66	
Obstt. & Gyn.	45	18	
Ophthalmology	16	8	
Orthopaedics	35	8	
E.N.T.	18	2	
Physical Medicine & Rehab.	2	1	
Community Health			
Community Health	13	7	
General Practice	16	9	
Total	496	206+(1 Result awaited)	

TABLE II

FINAL (PART II) MNAMS EXAMINATION FEBRUARY, 1979

GROUP	WRITTEN		PRACTICAL	
	No. Appeared	No. Passed	No. Appeared	No. Passed
A. Basic Medical Seiences	(* these figures include candidates failed inAugust 1978 (Practical)			
Pathology (Morbid Anatomy)	1	1	2*	2
Physiology	1	—	—	—
Microbiology (Bacteriology)	1	—	—	—
B. Medicine & Allied Sciences				
Medicine	21	12	15*	8
Paediatrics	14	6	6	3
Psychiatry	7	6	6	5
Dermatology	2	2	2	2
Radio-therapy	1	—	—	—
Radio-diagnosis	1	1	1	—
Anaesthesiology	8	6	9*	5
Respiratory Medicine	2	1	1	—
C. Surgery & Allied Sciences				
Surgery	21	20	24*	15
Obstett. & Gyn,	10	7	9*	2
Orthopaedics	6	3	4*	1
E.N.T.	4	3	3	1
Ophthalmology	3	3	4*	1
D. Community Health				
SPM	3	1	1	—
MCH	1	1	2*	2
Epidemiolology	1	1	1	1
General Practice	1	—	—	—
E. Medicine & Allied Sciences				
(Super Specialities)				
Cardiology	2	2	2	2
Neurology	1	1	1	—
Nephrology	1	1	1	1
F. Surgery & Allied Sciences				
(Super Specialities)				
Neuro-Surgery	2	2	2	—
Cardio-thoracic Surgery	4	4	4	2
Paediatric Surgery	1	1	1	1
Genito-Urinary Surgery	1	1	1	—
	121	86	102	54

Ann Natl Acad Med Sci (India), 15, 1, January-March 1979

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Ann Natl Acad Med Sci (India), 15, 2, April—June 1979

Functional Antibody Activities and Serum Immunoglobulin Levels in Cholera*

S. Bhattacharya, R.N. Majumder, A.K. Bose, B. Mondal and A.K. Ghosh

Division of Immunology and Serology, Cholera Research Centre (Indian Council of Medical Research), Calcutta 700016.

Revised received for publication, Oct. 30, 1978.

Quantitation of immunoglobulins, G and M, as well as of functional antibody activities was done in sera of acute and convalescent cholera patients. Basal serum immunoglobulin levels of normal adult Indians were also determined. Serum IgM level was elevated in acute phase of the disease, with a concomitant but much less rise of IgG. Both the immunoglobulins diminished over a 10 day period in cholera as compared to acute phase levels. Antibody activities, agglutinating, vibriocidal and passive haemagglutinating, were detectable in acute condition of the disease. and were further accentuated in convalescence without any elevated serum Ig levels.

Introduction

It is now increasingly felt that a simultaneous information of both the absolute immunoglobulin concentration as well as the functional activities of antibodies located therein is important in understanding the immune response of a host to a disease process, as "comparisons of antibody titres offer only a limited information, unless related to immunoglobulin concentration" (Newcomb et al, 1969). A number of workers in the past have measured the antibody titres in cholera (Pollitzer and Burrows, 1959; Felsenfeld, 1967; Feeley, 1972), and a report is also available on the immunoglobulin quantitation in this disease (Waldman et al, 1971), but no report is as yet available on measurement of both antibody titres and immunoglobulin concentration in the same group of cholera patients to give us a complete picture of the immune response in this disease process. The present study was, therefore, undertaken to evaluate the immune response in diarrhoeal patients of choleraic aetiology by (i) determining the serum immunoglobulin concentration as well as (ii) simultaneous measurement of serum antibody activities.

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*Paper presented at the Annual Scientific Meeting of the West Bengal Chapter of National Academy of Medical Sciences (India) held in December, 1977.

Material and Methods

Patients and sera : Cholera patients admitted in the S.B. Hospitals, Howrah, and in the I.D. Hospital, Calcutta, during the period from 25th May to 28th July, 1970, were included in the study. The patients were without a history of vaccination for the preceding 2 years.

Venous blood was drawn from the patients after initial rehydration, and serum specific gravity estimation by T.S. Meter (American Optical Company, U.S.A.) was done to check whether an apparent clinical rehydration was followed by normalization of haemoconcentration (Pierce **et al**, 1968). Sera from bacteriologically positive cholera cases (Ghosh **et al**, 1971) were included in this study. Paired blood samples were obtained on 10th day of illness. Sera were filtered through membrane filters (Millipore, USA, 0.45μ) and ampouled without any preservative and stored at —20°C till use.

Blood from healthy normal adults was obtained from the Blood Bank of the Institute of Postgraduate Medical Education and Research, Calcutta, as well as from local volunteers, and sera were processed and stored as above.

Quantitation of immunoglobulins : The concentration of immunoglobulins, G and M, was determined by radial immunodiffusion method (Fahey and McKelvey, 1965); using specific antisera to human IgG and IgM. The standard used was the WHO Standard Reference Preparation (NHS 67/97) with known concentration of IgG and IgM denoted in International Units, I.U./ml (Rowe **et al**, 1970). One I.U. of IgG denotes 80.4μg of IgG, and one I.U. of IgM 8.47μg of IgM. The immunoglobulin levels of the test sera have been expressed as I.U./ml as per the instructions laid down by the WHO International Centre for Immunoglobulins (Rowe **et al**, 1970; Group of International Experts, 1972).

Measurement of antibody activities : Agglutination and vibriocidal antibody measurements were done and the titres were expressed as reciprocal of the highest dilution of serum (Goodner **et al**, 1960; Finkelstein, 1962). Antigen used in the agglutination test were **V. cholerae** Inaba NIH 35A3 and Ogawa NIH 41, while vibriocidal antibody measurements were done using V. **cholerae** Inaba NIH 35A3 only, as both the V. **cholerae** serotypes give identical results in this test system (Finkelstein, 1962). Passive haemagglutination test was performed according to the technique reported by Ghosh **et al**, (1968), using cholera toxin (Wyeth, lot 001) as the sensitizing antigen, and titres similarly expressed. Cholera toxin was obtained from National Institute of Health, Md., U.S.A.

Results

Serum IgM was elevated in both the sub-groups (serum specific gravity > and < 1.028) of acute cholera patients with a minimal rise in the IgG levels (Table I). In convalescence, both the immunoglobulins registered a decrease as compared to the acute phase levels, though the IgM level in convalescent sera was still raised over the normal basal value.

Table I. Serum immunoglobulin (IgG and IgM) levels of normal Indian adults and choleraic diarrhoeal cases.

Group	Total no. of sera	Mean and standard deviation		P-value*		
		IgG I.U./ml	IgM I.U./ml	Groups compared	IgG	IgM
I (Normal)	60	104.4 ±3.39 (96-114)**	105.3 ±9.88 (80-126)	Normal vs. IIa	$P > .05$	$P > .05$
IIa (Acute cholera)	14	105.8 ±4.21 (95-112)	115.0 ±9.31 (96-132)	,, vs. IIb	$P < .01$	$P < .02$
IIb (Acute cholera)	45	106.6 ±4.51 (96-114)	110.7 ±10.8 (84-134)	,, vs. III	$p > .05$	$P > .05$
III (Convalescent cholera)	16	104.1 ±3.64 (97-108)	107.7 ±12.91 (82-128)	IIa vs. III IIb vs. III	$P > .05$ $P > .05$	$P > .05$ $P > .05$

* P-value taken from Fisher and Yates' Statistical Table.
$P < .05$ not significant; $P < .05$ significant

** Range
a) Serum sp. gr. < 1.028 b) serum sp. gr. > 1.028

Table II shows the functional antibody estimates in the respective groups; sera of both the sub-groups of the acute cholera patients are grouped together, as the titres in both were very much identical. Functional antibodies, agglutinating, vibriocidal and passive haemagglutinating, were detectable in acute phase sera. Convalescent cholera sera showed an increase in titres of all the three antibodies tested over the acute phase levels, of which rise of vibriocidal antibody was the most marked.

Table II. Functional antibody response in sera of choleraic diarrhoeal cases.

Groups	Number tested	Geometric mean titre (reciprocal)			
		Agglutinating antibody		Vibriocidal antibody	Passive haemagglutinating antibody
		Inaba	Ogawa		
Acute cholera*	42	17	23	83	100
Convalescent cholera**	14	55	85	2570	117

* within 24 hours post-onset
** on 10th day post-onset

Discussion

It has been reported that in cholera the level of serum IgM was significantly high althrough the course of illness from acute to four weeks, but without any change in IgG levels (Waldman **et al,** 1971). But in sampling of sera from patients, the workers relied on rehydration clinically assessed, but not substantiated by specific gravity determination. It is observed in the present work that specific gravity of serum may remain elevated even in apparently rehydrated cases. Again, Northrup and Hossain (1970) reported that in cholera, functional activities of both serum IgG and IgM rise in the course of disease, but the workers did not quantitate the serum levels of the antibody globulins. The present studies indicate a rise in both components of serum Ig, G and M, with that of IgM predominating, in acute cholera, followed by a fall in both over the 10 day period, though the IgM still remained higher than the normal level. However, when evaluated statistically, a significance was observed in the IgG ($P < .01$) and IgM ($P < .02$) rise in acute cholera (with high serum specific gravity) as compared to the respective basal level in normal adults. Though it is observed (Table I) that the IgM level in acute cholera cases (with normal serum specific gravity) attained a higher level, the result has not been found statistically significant, and this is presumably due to non-equivalance in numbers of the study population. No difference, significant statistically, was observed between the Ig levels, G and M, in convalescent cholera as compared to the respective levels in both the subgroups of acute cholera ($P > .05$). As regards the basal immunoglobulin levels in normal Indian adults, some earlier reports are available (Sehgal and Aikat, 1970; Samuel **et al,** 1970). But in view of the fact that "highly significant heterogeneity of estimates between laboratories" exist (Rowe **et al,** 1970; Group of International Experts, 1972), basal serum immunoglobulin levels in local population were worked out under the same experimental conditions as the test samples.

Functional activities of antibodies, as measured by the three serological parameters mentioned above, were present in a detectable level in acute phases of cholera and were further elevated in convalescence, of which rise in vibriocidal antibody response appears to be significant. This corroborates the findings of earlier workers (Kasai and Burrows, 1966; Sack **et al,** 1966). However, the present study indicates that with serum Ig levels not much altered, the functional antibody activities have shown wider fluctuations over a 10 day period in cholera, the reasons of which remain to be explored (Fig. 1). Similar trends were observed by us in other studies, and might have reflected the difference in relative sensitivities of the two test systems, quantitation of Ig being a precise assay against known standard and tests for functional antibody a semiquantitative one, more prone to subjective variation (Bhattacharya and Ghosh, 1976). The quantum and the trend of the immune response in cholera as reported and discussed above signify glimpses of a rapidly passing phenomenon as reflected on the immune system of the host. However, the clinical significance of the rise of immunoglobulin in sera of patients with acute phase of cholera may be attributed due to access of soluble antigen of **V. cholerae** (soluble cell wall antigens and extracellular cholera toxin) to the immune system of the host, although, **V. cholerae,** the organisms as such are not accessible to that system (Bhattacharya and Ghosh, 1975). It is quite rational to think that as soon as the source of antigenic stimulus is cut off (host becomes bacteria free when the acute phase of illness is over), the elevated level of Ig starts coming down to normal. But the left over memory in

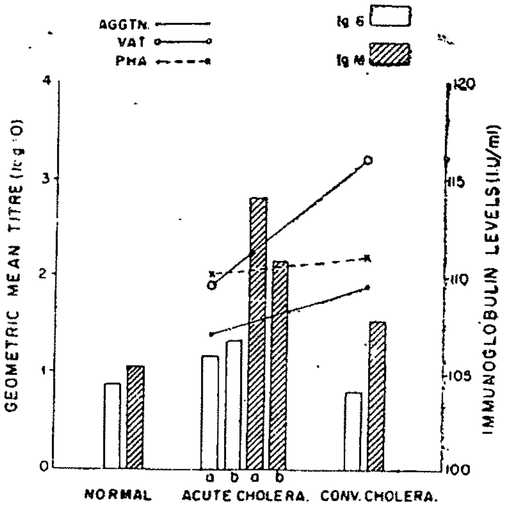

Fig. 1. Immunoglobulin and functional antibody concentrations in sera of acute and convalescent cholera patients.

a = sp. gr. < 1.028 **b = sp. gr. > 1.028**

the host's immune system persists for certain period of time (during convalescence) which is evident by the rise of the functional activities of the antibodies as measured by different tests parameters used in this study.

Acknowledgements

The authors wish to thank Dr. S. Mukerjee, the then Director of Cholera Research Centre, for his help and encouragement in carrying out the study, and Drs. H.C. Goodman and D.S. Rowe, World Health Organization, Geneva, Switzerland, for supply of specific antisera to human IgG and IgM and the Standard Serum (NHS 67/97).

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The Effect of Distending Superior Vena Cava Right Atrial Junction on Urine Flow in Dogs

J.L. Agarwal and P. Seth

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Introduction

Two types of nervous structures are present in the atrial endocardium of the dogs. They are present throughout the atrium, but are most abundant at the junction of veins with atrium (Nonidez 1937, Miller and Kasahara 1964). It has been demonstrated that atrial receptors are intimately involved in the regulation of salt and water balance of the body. Stimulation of left atrial baroreceptors by increase in atrial pressure has been shown to increase urine flow, urinary sodium excretion (Henery **et al** 1956) and decrease in anti diuretic hormone level, while the increase in right atrial pressure also resulted in diuresis, but without the decrease in anti-diuretic hormone level, while there was a significant decrease in renin concentration (Brennan **et al**, 1971). So it appears that the mechanism of action of both these receptors are different. Arndt **et al** (1963) attributed this response to renal haemodynamic changes, while Henery and Pearce (1956) attributed the occurence of diuresis to stimulation of atrial receptors and demonstrated that their afferent path way lies in the vagi.

The relationship between diuresis and blood pressure is not well understood which is observed by distending superior vena cava-right atrial junction. In the present study an attempt has been made to show the effect of distension of superior vena cava-right atrial junction on urine flow and blood pressure and its possible nervous mechanism.

Material and Methods

Ten stray healthy dogs of both sexes weighing between 10-15.4 kgs. were employed in the present study. Sodium pento barbitone (Nembutal, Abbots lab. India) was injected intraperitoneally (30-40 mg/kgs. body weight) to induce anaesthesia. Normal saline 0.9 per cent sodium chloride) was started as intravenous drip at the rate of 15 drops/min. to keep the dog hydrated.

After the induction of anaesthesia a mid line incision was made in the neck of expose trachea and carotid sheath for dissecting vagi. Trachea was cannulated, and artificial respiration was started with respiratory pump running at the speed of 18 rev./min. with inspired volume maintained at 30 ml/3 kg. body weight.

A mid line incision was made in the abdomen to expose bladder and ureters. Ureters were catherized and connected to the drop recorder.

The right side of the chest was opened through 4th intercostal space. A foley's catheter (Paediatrics No 8) was inserted through external jugular vein into superior vena cava. The balloon was placed at the junction between superior vena cava and right atrium. Purse string suture were applied to prevent the balloon from displacement. Superior and inferior vena cava were shunted to maintain the venous return. Heparin (500 i.u.) i.v. was injected to prevent the blood clotting.

Blood pressure was recorded through femoral artery connected to mercury manometer. Rectal temperature was maintained at 37 ± 1°C.

The experimental protocol used for the experiment was as followed. After a period of equilibrium following surgery (about 1 h.), blood pressure was recorded for 1-2 min. and urine flow for a period of 30 min. Then the superior vena cava-right atrial junction was distended first with 4 ml. warm saline (37°C) by the tube to inflate the balloon. Blood pressure was recorded after 2, 5 and 10 min. for a period of 1 to 2 min. whereas the urine flow was measured after 10 min. for a period of 30 min. Then balloon was further distended with 8 ml. and 12 ml. saline. Blood pressure and urine flow were recorded in the same manner. Then the distension was relieved.

Both Vagi were blocked by Cooling at 5°C and balloon was distended with 4 ml. saline. Recordings were taken in the same way.

Then Vagi were rewarmed. Intravenous injection of propranolol hydrochloride (Inderal 0.5 mg./kg.) the β- adrenergic blocker, and bretylium tosylate (10 mg./kg.) the adrenergic neuronal blocker were used to block the effects of sympathetic nerves. Then superior vena cava-right atrial junction was distended with 4 ml. saline and blood pressure and urine flow were recorded.

The urine flow was recorded for 30 min. and average of urine flow drops/min. were calculated. Blood pressure was recorded at 2, 5 and 10 min. after distension and mean blood pressure was calculated and analysed.

Results

In the ten dogs when recording commenced after equilibrium has established the blood pressure was 133.9 ± 15.1 mm. Hg. and urine flow was 8.1 ± 2.28 drops/

min. When superior vena cava right atrial junction was distended with 4 ml., 8 ml. and 12 ml., the change in blood pressure were inconsistent and statistically insignificant.

However urine flow changed to 12.2 ± 2.66 ($P<.01$), 13.7±2.87 ($P< .05$) and 15.5 ± 2.46 ($P < .001$) drops/min. after distension with 4 ml., 8 ml. and 12 ml. saline respectively. The changes in urine flow were statistically significant and increased with increasing distension.

In order to determine the afferent path way of the response the effect of cooling vagi on change in urine flow and blood pressure were studied. When vagi were cooled at 5°C the blood pressure and urine flow were 142.6 ± 11.82 mm. Hg. and 8.2 ± 2.56 drops/min. and changed to 139.8 ± 9.09 mm. of Hg ($t = 0.69$, $P > 0.5$) and 8.1 ± 2.42 dsops/min. ($t = .03$, $P > 0.5$) respectively. From these results it is concluded that the afferent path way of this reflex diuresis is in vagus nerves.

To establish whether the observed increase in urine flow was due to sympathetic effect. The effect on urine flow by blocking transmission of sympathetic nerves were studied. The urine flow changed from 10.6 ± 2.46 to 13.8 ± 3.22 drops/min. ($t = 1.56$, $P > 0.1$). In experiment in which sympathetic activity is blocked, there is still an effect on urine flow (30 per cent) of course statistically less than that of without sympathetic blockage (51 per cent) with 4 ml. saline. These results concludes that diuresis caused by streching superior vena cava right atrial junction is perhaps not due to change in sympathetic activity to the kidney.

Discussion

Insignificant and inconsistent changes in blood pressure were recorded on distending superior vena cava right atrial junction. These observations confirmed the finding of earlier workers (Kappagoda **et al** 1970, 1972 a). Brennan **et al** (1971) also reported that when right atrial pressure was increased by 6 mm. of water, the mean arterial pressure remained essentially unchanged.

Distension of superior vena cava-right atrial junction resulted in marked diuresis with 4 ml., 8 ml. and 12 ml. distension which was found to statistically significant ($P < .01$, $P < .05$, $P < .001$), (Table I). When distension was increased step wise the diuretic response increased 51 per cent with 4 ml., 69 per cent with 8 ml. and 90 per cent with 12 ml. distension. These observations are in agreement with those reported by earlier authors (Kappagoda **et al** 1973), who reported that the stretching of the junction between superior vena cava-right atrium resulted in an increase in urine flow with 10-16 ml. normal saline and attributed this response to reflex caused by stimulation of right atrial receptors. However they found a smaller response (18 per cent) with superior vena cava-right atrial junction distension then when atrial appendages were distended (34 per cent). The response on urine flow by distending superior vena cava-right atrial junction was found to be greater than that by distending atrial appendages (Agarwal **et al** 1978). This may be due to more number of receptors present at veno-atrial junction (Miller and Kasahara 1964).

Table I. Effect of distension of superior vena cava right atrial junction on blood pressure and urine flow.

Measurements	Control ± SD	During Distension of S.V.C.=right atrial Junction					
		Distension with 4 ml. saline mean ± S.D.	't' Value	Distension with 8 ml. saline mean ± S.D.	't' Value	Distension with 12 ml. saline mean ± S.D.	't' Value
Blood pressure in mm of Hg.	133.9 ± 15.1	133.8 ± 13.61	0.015 $P > .5$	132.1 ± 12.91	0.28 $P > .5$	13.6 ± 11.93	0.23 $P > .5$
Urine flow drops/min.	8.1 ± 2.28	12.2 ± 2.66	4.14 $P < .01$	13.7 ± 2.87	2.75 $P < .05$	15.5 ± 2.46	7.71 $P < .001$

Cooling of Vagi abolished diuretic response to superior vena cava-right atrial junction distension with 4 ml. saline (Table II). Kappagoda **et al** (1972 b) reported similar response on cooling the vagus nerves. Henery and Pearce (1956) also observed that the diuretic response to stimulation of atrium is abolished by cutting vagus nerves, and attributed it to the atrial receptors.

Table II. Effect of distension of superior vena cava right atrial junction on blood pressure and urine flow after cooling vagi and administring propranolol HCI and bretylium tosylate.

Measurements	After cooling Vagi			After administration of propranolol HCl and bretylium tosylate		
	Control mean ± S.D.	During distension with 4 ml. saline mean ± S.D.	't' Value	Control mean ± S.D.	During distension with 4 ml. saline mean ± S.D.	't' Value
Blood Pressure in mm of Hg.	142.6 ± 11.82	139.8 ± 9.09	0.69 $P > .5$	128.4 ± 10.26	111.4 ± 15.7	1.27 $0.1 < P < .5$
Urine flow drops/min	8 2 ± 2.56	8.1 ± 2.42	0.03 $P > .5$	10.6 ± 2.46	13.8 ± 3.22	1.56 $0.1 < P < 0.5$

Kappagoda **et al** (1972 a) reported that atrial appendages distension produces diuresis and reflex arises from the receptors situated in atrial appendage. Miller and Kasahara (1964) demonstrated that the receptors in atrial appendages and the superior vena cava-right atrial junction are of same type, while they are more abundant at veno-atrial junction. The increase in urine flow after distension of superior vena cava-right atrial junction could be attributed to participation of atrial receptors present at veno-atrial junction (Floyd **et al** 1972). This could also be due to mechanism which regulate the size of the heart within narrow limits firstly because of its effect on heart rate (Kappagado **et al** 1972 a) and secondarily by its effect on Kidney and volume of extra Cellular fluid (Brennan **et al** 1971).

When sympathetic blockers were administered the urine flow was found to be 10.6 ± 2.46 drops/min. and increased to 13.8 ± 3.22 drops/min. after distension. Brennan **et al** (1971) reported that receptors located on the right side of the low pressure system do not have a controlling influence on ADH secretion, while they causes a reduction in renin secretion by kidney. Genest **et al** (1968), found that the increase in right atrial pressure resulted in a rise in renal vein renin activity. Anderson **et al** (1959) noted a fall in the plasma level of aldosterone when the right atrium was stretched but not the left.

It is known that β-adrenergic blocking drugs antagonizes the release of renin from Juxta glomerular apparatus of the kidney (Ganong 1973), by sympathetomimetic amines or sympathetic nerve activity. They also reduce but not completely block the increase in plasma renin activity induced by sodium deprivation (Michelakis and Mc-Allister, 1972).

So it is clear that the diuretic response to the distension of superior vena cava-right atrial junction is not mediated by the sympathetic nerves to the juxta-glomesular apparatus to regulate the renin release, as potsulated by Brennan **et al** (1971), but by some other mechanism, possibly humoral mechanism mediate this response.

From the above work presented here it is evident that stretching superior vena-cava-right atrial junction leads to diuresis without any significant change in blood pressure. We presume that diuresis is the result of some reflex initiated by stretch of superior vena cava-right atrial junction and afferent path-way is in vagus. Sympathetic blockage don't abolish the response so we presume that the response is mediated through some humoral mechanism to the kidney to regulate either renin release by juxta-glomerular cells or possibly by some other hormonal factors.

Conclusion

Distension of superior vena cava-right atrial junction evokes diuresis without any appreciable changes in blood pressure. This diuretic response is due to reflex initiated by stimulation of receptors present at superior vena cava-right atrial junction. The afferent pathway of the reflex is in vagi as cooling of Vagi abolishes the diuretic response, but efferent path way is not perhaps in the sympathetic nerves to regulate the renin release.

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A Mathematical Model for the Detection of Hypertension

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The discriminant analysis of statistical theory was applied to develop a model for the classification of hypertensive and non-hypertensive patients. Various factors responsible for hypertension and their relative effect on the incidence of hypertension have been discussed by a new approach. By the help of various statistical tests an attempt has been made to prove the validity and usefulness of the model. Various alternatives have been discussed and some improvements have been suggested. The study as well as the analysis rests heavily on the advanced multivariate analysis.

Introduction

In a number of previous studies, the dependence of hypertension on more than one factors has widely been recognised and various socio-economic, personal and demographic factors **viz,** mental tension (Henry and Cassel 1969; Leigh 1971), heredity (Pickering 1967; Platt 1967), age and sex (Indrayan **et al** 1972a; Gordon 1964), body built (Sive **et al** 1970), socio-economic status (Indrayan **et al** 1972b) and weight (Miall **et al** 1968; Florey and Acheson 1969; Srivastava **et al** 1977) has been associated with it. But little or no progress has been made towards analysing this association. Thus relative effects of various factors affecting the hypertension are still to be analysed. Naturally such type of analysis will be of great importance in the prevention of hypertension though not necessarily in the cure of it. As far as our knowledge is concerned, we have not come across any such type of study.

Besides this there are other problems too that are faced in the treatment of hypertension. Even after prolonged and continued efforts we are still not able to provide sufficient health facilities to the population, specially to the rural one. As the diagnosis of hypertension requires the aid of certain instruments that can be used only by a well trained and qualified person, the problem becomes more serious. In villages we are still not able to provide a qualified and well equipped doctor with a dispensary and most of the village population is suffering with the lack of minimum medical care. This is also one of the major factors for the various superstitions and blind beliefs that are in vogue in the rural population. Hence the need is of some diagnostic method which can be helpful in rural population and is free of any technicalities so that it can be used by paramedical persons. Such type of method can be of much help to the success of community health worker and bare foot doctor schemes of the Government of India, Ministry of Health and Family Welfare.

The basic idea behind the evolution of such type of method is that of model building, a mathematical model. Such types of models have widely been used in the control of various communicable diseases and in the field of epidemiology. The fundamentals behind the model construction can be explained by the following discussions on hypertension : Every person in a population will always be in any of the two groups, the hypertensive one and the non-hypertensive one. The problem of diagnosis of hypertension therefore reduces to that of classifying a person into two groups, the hypertensive and the non-hypertensive one. This classification is made possible by the use of correlation or association that exists between various factors affecting hypertension and the hypertension itself.

Naturally such type of model construction is always associated with some error. The main importance of the model construction is that we can always measure this error and by giving some concession to precision this error can be confined to certain predefined limits. Thus the use of the model divides the population into two classes, one susceptible to hypertension and the other not. Once the population has been divided into two groups it becomes easier as well as economical to concentrate the efforts to the susceptible population only. Thus in addition to detection such type of models help the planners in the maximum utilization of their limited resources. This paper therefore aims at developing a model that can classify the population into two groups as discussed and then to analyse the relative effect of various factors on hypertension.

Material and Methods

The study is based on the data obtained from the records of J.A. Group of Hospitals, Gwalior. A Blood Pressure Detection Clinic is run by the department of Preventive and Social Medicine, G.R. Medical College, Gwalior in the out patient department of the hospital in which various informations regarding the factors associated with hypertension are recorded. The systematic sampling was applied to the recorded data and a sample of 900 was selected out from a total registration of 9175 cases. The sample so selected was divided into two groups, the hypertensive one and the non hypertensive one. There were 214 cases in the hypertensive group and the remaining cases in the non-hypertensive group. As it is the dystolic blood pressure only which causes a number of complications when increased, the criteria for hypertension was taken to be 90.00 mm. of Hg for the dystolic blood pressure. An individual with a dystolic blood pressure greater than 90.00 mm. of Hg was included in the hypertensive group.

Four variables viz. Age, Socio-economic status, Number of children and the Standing height were taken up for the study. The grades for the socio-economic status was allocated by using the Lickert's method of scaling or what is known as the category method of scaling with the assumption of normality of the population.

First of all the student's 't' test was applied between the mean values of age, socio-economic status, number of children and standing height of the groups in order to test the significance of the difference between the two groups. At this point it should be pointed out that in usual test of significance, the level of significance is generally taken as .05 or .01 but in case of selection of variables for discrimination or classifying purpose the level of significance can not be taken as .05 or .01 as this may result in serious loss in terms of discriminating power of the model. Actually in such cases, the level of significance should be .50 in place of .05 in order to take into consideration almost all the variations in various variables. As the P value for standing height was greater than .50, this variable has been left out of the study. After selecting out the various factors in the above manner, the discriminent analysis (Khirsagar 1974; Rao 1973; Prem Narain and Garg 1975) was applied to obtain a model for classification. The values of Mahalanobis D^2-statistic was calculated for analysing the relative effects of various factors and for testing the various features of the model.

Results

The arithmatic mean, range and standard deviation for age, socio-economic status, number of children and standing height for the two groups are compiled in Table 1. According to the discussions of Rao (1952) a linear model was constructed. The optimum values of discriminent function and the relative contribution of each of the factors age (X_1), socio-economic status (X_2) and number of children (X_3) are compiled in Table II. The discriminent function was found to be

(A) $Y = 2.288\, X_1 - 36.168\, X_2 + 18.920\, X_3 - 125.694$

and the classification procedure becomes

(i) Calculate the value of Y from (A) by putting the values of X_1, X_2 and X_3 for any individual.

(ii) If $Y > O$ classify the individual in the hypertensive group, otherwise in the non-hypertensive group.

Table I

Factors		Hypertensive group	Non hypertensive group	s.e.	't'	P
1. Age	Mean	48.43	36.13	3.42	3.47	< .001
	Range	82-20	75-20			
	S.D.	15.66	14.00			
2. S.E. Status	Mean	2.45	2.89	0.23	1.91	< .01
	Range	5-1	5-1			
	S.D.	1.03	1.04			
3. Number of children	Mean	7.10	6.18	0.70	1.31	< .20
	Range	20-2	12-2			
	S.D.	3.52	2.02			
4. Standing height	Mean	62.79	63.54	1.70	0.44	> .50
	Range	70-56	73-56			
	S.D.	3.86	12.07			

Table II

Character	Coefficient	Contribution value	%
1. X_1 = Age	2.288	27.94	45.61
2. X_2 = S.E. status	—36.168	15.91	25.97
3. X_3 = Number of children	18.920	17.41	28.42

For example if the values of X_1, X_2 and X_3 for any individual after proper grading are 56, 1 and 4 respectively then from (A) we get

$$Y = 41.95$$

and we classify the individual in the hypertensive group.

Finally 'F' test was applied to test whether any variable can be deleted from the model and the results are given in table 3 which shows that none of the variable can be deleted from the model.

Discussion

In accordence with a number of previous studies it is proved that hypertension is associated with age and socio-economic status (Indrayan **et al** 1972a; Indrayan et al 1972b) but not with the number of children in the family. However because of the discussions above this variable has also been taken up for study. It will be seen later on that the inclusion of this variable increases the discrimination of power of the model to a significant extent and this automatically justifies the inclusion of this variable in the study.

The equation (A) and the classification procedure described therein suggest the possible nature of decision making. As is apparent, such type of decision making is of much help at the primary level where advanced medical facilities either can not be provided or are difficult to be provided. By the help of such type of models we can divide the population into susceptible and non-susceptible groups thus utilizing the limited resources upto maximum extent.

The relative discriminating power of each variable is compiled in Table II and in Table III the values of D^2 after deleting a variable has been compiled. It is clear from Table III that all the variables taken up for the study are important from discrimination point of view and so none can be left out. It is also clear from Table II that the discrimination power of age is approximately twice that of socio-economic status or number of children. This concludes that the effect of age, socio-economic status and number of children is in the ratio 2 : 1 : 1. Thus the discriminating power of number of children is again clear and though the difference between hypertensive and non-hypertensive groups is not significant, a high discriminating power justifies the inclusion of the variable in the study.

An interesting feature is observable from Table II. It can be seen that the coefficient of socio-economic status is negative showing that the hypertension and socio-economic status are negatively correlated. This proves that hypertension is the phenomena associated generally with the upper socio-economic group.

The above analysis reveals the wide scope of the tools in clinical as well as public health problems. The method developed can be of very much help in tackling

Table III

Character left out	D^2 based on remaining factors	Variance ratio	P
1. Number of children	43.85	51.9447	$< .001$
2. Socio-economic status	45.35	63.1981	$< .001$
3. Age	33.32	7.2156	$< .001$

the problems of rural population. However being population based and cross-sectional, the study has some drawbacks in terms of omissions of certains factors from the study. This however in no way reduces the power and verstality of the tools applied. It is hoped that such type of analysis will be of great help in both clinical and public health problems.

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Roentgen Features of Lipomas of Extremities

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Roentgen features of 6 cases of deep seated lipomas of extremities are reported. In addition to chracteristic radio-lucency seen on radiographs, two parosteal lipomas showed bowing of bone, reactive sclerosis and minimal hyperostosis in one case. In one case there was separation of superior tibio-fibular joint. One case of lipoma in the thigh had a rare feature of extensive areas of ossification and calcification.

Introduction

Lipomas occur in any location of the body but perhaps are most commonly found in the subcutaneous regions where there is relatively more adipose tissue (Jacobs 1972). Lipomas situated with in or deep to the muscle are relatively uncommon and are difficult to diagnose on clinical examination. Radiologic appearance of well defined radio-lucent zone in contrast to more opaque shadows cast by surounding soft tissue first described by Kohler (1915) give us a certain diagnosis. Other less reported but important roentgen diagnostic features of deep seated lipomas of extremities are bowing of bones, pressure erosion of subjacent bone, sclerosis of bony surfaces hyperostosis and areas of calcification and ossifications (Fleming et al 1962, Greenfield 1969, Jacobs 1972, Kenin et al 1959, Murphy 1974).

We in this communication are reporting roentgen features of 6 cases of deep seated lipomas of extremities, two of which were parosteal in location and one had extensive areas of calcification and ossification.

Observations

In two cases lipomas were sub-deltoid in location, in two they were in the thigh in one in the upper forearm and in another in the leg deep to the calf muscles.

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PLATE I

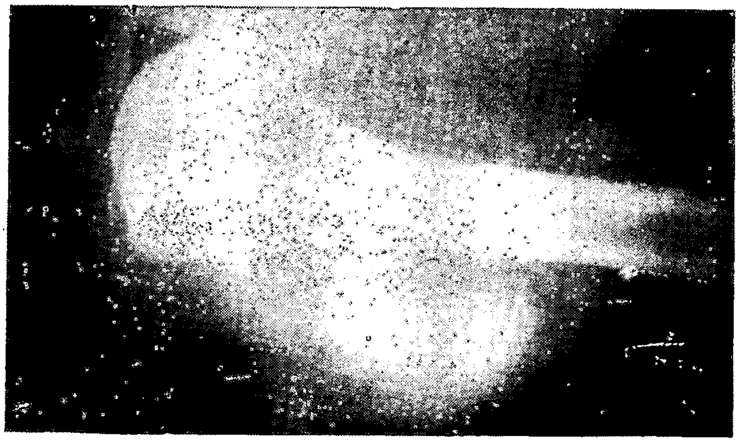

Fig. 1. X-ray of right shoulder joint showing well defined radiolucency of subdeltoic lipoma.

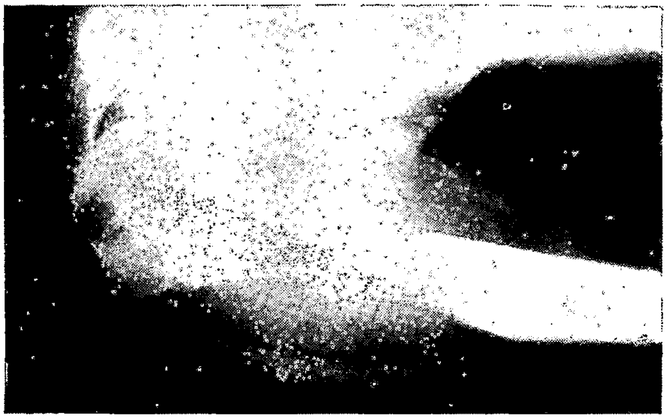

Fig. 2. X-ray of shoulder showing subdeltoid parosteal lipoma causing concave pressure deformity of humerus and uniform marginal sclerosis.

PLATE II

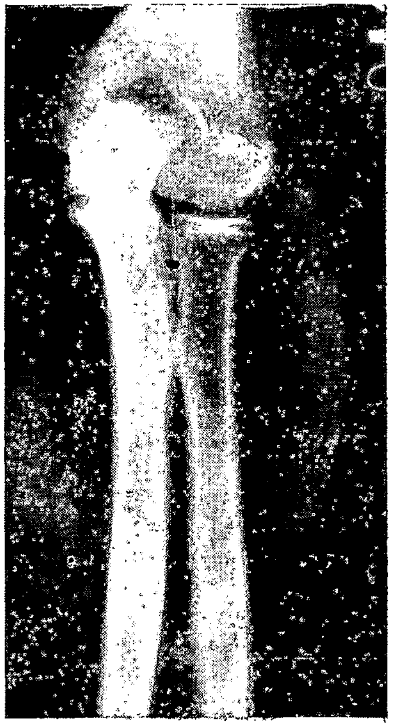

Fig. 3A. Skiagram of forearm showing characterstic radiolucency of lipoma, pressure deformity of ulnar shaft and minimal reactive sclerosis (arrow).

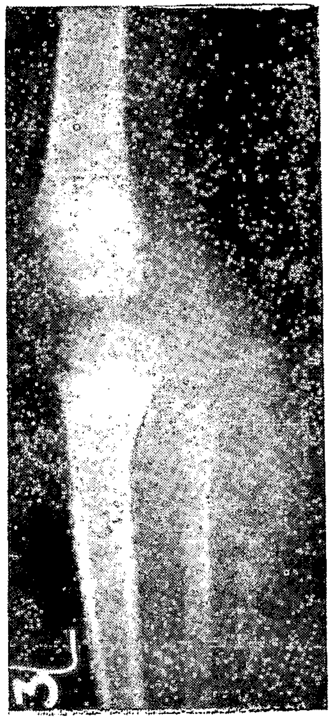

Fig. 3B. X-ray of upper leg showing separation of fibula and tibia.

PLATE III

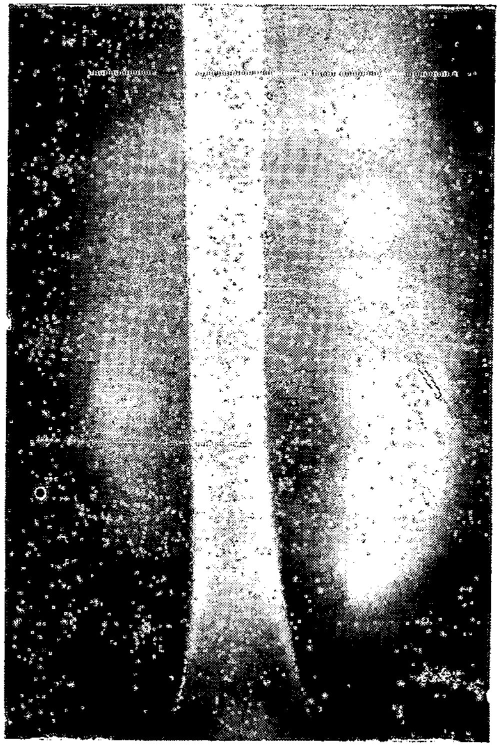

Fig. 4. Skiagram of thigh showing characteristic radiolucency of multilobulated large size lipoma.

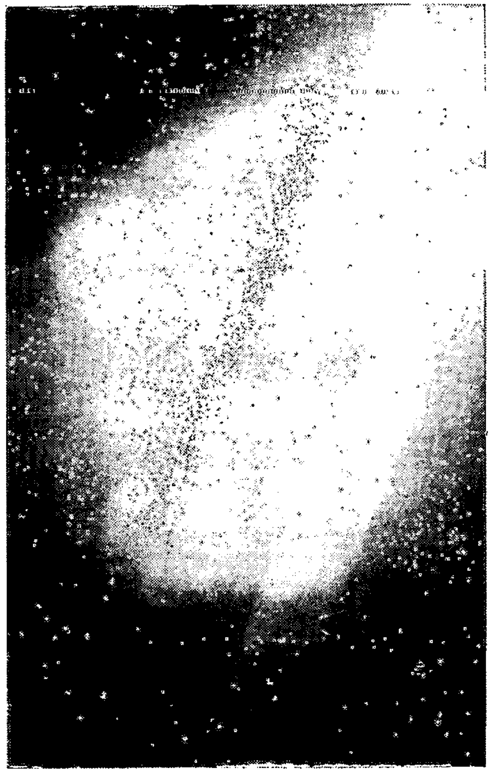

Fig. 5. X-ray of thigh showing large masses of homogeneous calcified and ossified masses in a huge soft tissue mass.

All cases had chracteristic radiolucency in contrast to surrounding soft tissues (Plates I to III, Figs. 1 to 5). One of the lipoma in the shoulder region had concave pressure deformity of underlying humerus with reactive uniform cortical sclerosis (Plate I, Fig. 2). The case of forearm lipoma produced bowing of ulna and cortical sclerosis as well as minimal hyperostosis (Plate II, Fig. 3A). Obviously lipomas in these two cases were situated next to the bone that is parosteal in location. One case of lipoma of thigh showed large lobules of adipose tissue separated by septa (Plate III, Fig. 4). The other case of lipoma in the thigh showed areas of calcification and ossification (Plate III, Fig. 5). Separation of superior tibio-fibular articulation was seen in the lipoma of the leg (Plate II, Fig. 3 B), All the patients were operated upon and diagnosis of benign lipoma was confirmed histologically. In two cases (Plates I and II, Figs. 2 and 3 A) on exploration the lipomas were found to be fixed to the underlying bones. The case of calcified and ossified lipoma of thigh revealed fair amount of fibrous tissue on histologic examination. Clinical diagnosis of lipoma was suspected only in one case (Plate III, Fig. 4) where a large part of lipoma was also palpable subcutaneously.

Discussion

Consistency of lipomas of extremities when situated with in or deep to the muscles is often difficult to evaluate clinically because of overlying muscles. However, their characteristic radiolucency in contrast to surrounding soft tissue allows the radiologist to give a certain diagnosis. The degree of radiolucency depends upon the amount of adipose tissue. Well defined radiolucent lesions indicative of little if any fibrous tissue are usually benign (Sutton, 1969). If a large fibrous component is present, the density may be indistinguishable from the neighbouring soft tissues. Fibrosarcoma containing considerable amount of nonfatty fibrous tissue is less well defined and radiolucent. Our case (Fig. 5), showing ossification and calcification had fair amount of fibrous tissue in addition to prenominance of adipose tissue on histological examination, and that is why areas spared of calcification did not show classic radiolucency of lipoma.

Some lipomas occur in close relationship to the long bones and are called parosteal lipoma. Precise origion of these lipomas is uncertain. They probably do not arise from the periosteum since no fat tissue is present in the cambium cells of periosteum. They are firmly attached to the cortex of underlying bone but are amenable to complete surgical removal (Jacobs 1972). Additional radiologic features of parosteal lipomas are bowing or deformity of bone, sclerosis of bony surfaces and hyperostosis (Fleming **et al** 1962 and Jacobs 1972). Pronounced associated hyperostosis is extremely uncommon and is probably caused by stimulation or irritation of periosteum (Fleming **et al** 1962, Jacobs 1972 and Kenin **et al** 1959). This marked hyperostosis may resemble, osteosarcoma. However, presence of well defined radiolucency of adipose tissue is so characteristic that no difficulty should arise in differentiation (Jacobs 1972). Two of our cases (Fig. 2 and 3 A) belonged to this category but without marked hyperostosis.

Calcification and ossification of lipoma is a rare feature reported only twice earlier (Murphy 1974 and Plamit et al 1967). Ossification does not indicate malignancy and is regarded as metaplastic change which has arised from pre-existing fibrofatty mesenchymal elements (Plamit et al 1967). Lichenstein (1965) has stated that he knows of no case of benign lipoma becoming malignant and bone production is very rare in a malignant fatty tumour.

Ossifying lipoma must be differentiated from tumoral calcinosis which occur as large calcified painless masses situated in the vicinity of joints predominantly on the extensor surfaces. Calcification is nodular and is of greater density than in the ossifying lipoma and tends to increase in amount, longer the lesions is present (Harker and Pellears 1967).

This tumour is important to the radiologist who can give a spot diagnosis. Indeed this must be one of the few tumours which affect the bone and there can be no dispute concerning the radiographic or histologic appearances.

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*The MRCP (UK) System

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The three Royal Colleges of Physicians in the UK (London, Edinburgh and Glasgow) have had a common Membership examination for nearly ten years. Previously there had been three separate MRCPs, each examination being different. Thus, at Edinburgh you could take your Membership in a special subject, in London you could not.

In 1968 the Colleges set up a common Part I examination and in 1972 a common Part II. The Membership is now identical whether you take it in London, Edinburgh or Glasgow and there is now only one designation for those who have passed it, MRCP (UK).

Part I consists only of a multiple choice paper. The object is to test factual knowledge and act as a screen so that unsuitable and unprepared candidates do not go further in the Examination. Part I cannot be taken until a candidate has been qualified for at least eighteen months. In the UK this means in effect that he must have completed his pre-registration house appointments and done one further job. Part I can be taken in several centres in the UK and abroad, for example it is held in Hong Kong, Baghdad, Cairo, Colombo and Accra as well as other places. New centres for Part I are likely to be created in the future.

Once a candidate has passed Part I he can attempt Part II at any time. Part II is held only in the UK and takes place three times a year. It consists of three parts, written, oral and clinical. The written part is held in the Colleges and comprises case-histories for analysis, problems in data interpretation, e.g. pathology reports, and projected material, when photographs, x-rays, histological sections, etc. are shown on a screen and the candidates attempt to interpret them.

A few weeks later the orals and clinicals are held. These are completed in one week and each candidate usually does his oral and clinical on the same day. In London the orals are held in the College in the morning, the clinicals in the hospitals in the afternoon. Early this year the London College started to hold the oral and clinical parts of the Part II examination in a provincial centre (Sheffield) as well as in the London hospitals and this practice will continue at different provincial centres in the future.

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* The paper is based on a talk delivered under the auspices of the Academy on Dec. 11, 1978, at the A.I.I.M.S., New Delhi.

** Registrar and Physician.

In the oral examination the candidate meets a pair of examiners and sometimes an extra specialist examiner such as a neurologist or dermatologist. He may be asked questions on any aspect of medicine, predominantly on clinical subjects.

There are two parts to the clinical examination. The first is a long case when the candidate has an hour to take a history and complete a physical examination being questioned on his findings and their interpretation by a pair of examiners for 20 minutes. They will usually ask him to demonstrate the physical findings. In the other section of the clinical examination he will be shown three, four or more short cases where he will be asked to examine one particular part of the body, e.g. a heart, optic fundus or a hand, and come to a conclusion. In these cases there are always definite physical signs and the candidate will be expected to detect and understand them.

Since 1977 paediatric candidates have had an entirely separate part II examination. The pattern is the same as for the adult medicine examination but it is conducted by paediatricians on children. No distinction is made in the designation given to successful candidates; MRCP (UK) may be in adult or paediatric medicine.

The MRCP is a test of clinical competence and it is therefore essential to pass the clinical part of it. Nothing can redeem a clear failure in the clinical examination. This fact needs to be constantly emphasised. Any candidates who fail in the examination do so because they do badly in straight forward clinical medicine, not because they are ignorant of the minutiae of medicine; that it not likely to be fatal but clinical inexperience or incompetence is. Sometimes candidates are tempted, perhaps by having passed the Part I easily, to go on to the Part II quickly. It is essential to have a proper grounding in clinical medicine before attempting the Part II, any weakness in this respect is likely to be quickly exposed in the examination. If a candidate is rough or inconsiderate in the clinical examination this will not find favour with the examiners.

A young doctor who is proposing to take up say radiology or pathology and thinks he would like to "have a go" at the Membership would be well advised to make sure that he has had enough training in general medicine before doing so. Reading books is not enough.

Two warnings : a candidate may attempt the Part I only four times and the Part II only six times. No exception to these rules is made. Further more if a candidate does badly in Part II he may be referred for one or two further examinations, i.e. he is not allowed to take the examination again for perhaps a year. This can be a hardship for a candidate from abroad who may be proposing to stay in the UK for only a limited time.

The pattern, structure and function of the Membership examination is kept under constant review by the three Colleges. Careful records are kept of candidates' performance (and examiners'). Certain key questions are used to act as markers of standards to see how performance at one time and in one place compares with those at others. There is interchange between examiners of the three Colleges and between examiners in the adult and paediatric parts of the examination.

The present examination is not immutable, but whatever changes may come it is inconceivable that the Membership will ever be anything but a rigorous test in clinical medicine.

The MRCP (UK) gives a mark of approval to those young doctors who by their ability, training and experience are ready to go on to higher, usually specialist, training and ultimately to the practice of hospital medicine. It is now essential for those who aim to practice as consultants in general medicine or its sub-divisions in the UK to pass this examination. Possessing the Membership does not mean that a man is a qualified specialist, it means only that he is ready for higher training. The Membership is an "entry" not an "exit" examination, i.e. entry into higher training not exist from it. Some overseas doctors having passed the MRCP (UK) return to their own countries and represent themselves as of consultant status. This is wrong and shows a misunderstanding of the purpose and status of the Membership.

I conclude by repeating the caution I gave earlier. The Membership examination of the three Royal Colleges of Physicians in the United Kingdom is a searching test of clinical medicine. No amount of abstruse theoretical or up-to-the-minute information can compensate for clinical inadequacy. Candidates should not attempt it until they have had proper training and experience in general medicine and in the opinion of their seniors have a reasonable chance of passing. If they do attempt the examination when inadequately prepared they are likely to be disappointed and—since they must come to Britain to take Part II—they may be put to considerable trouble and expense.

Ann Natl Acad Med Sci (India), 15, 2, April-June 1979

N.B.E. News

Recognition of Pre-1976 MAMS qualification : As reported earlier in the January-March 1979 issue of this journal a special examination (Interview), as agreed to by the Medical Council of India and the Govt. of India, was held on May 4 and 5, 1979, for the pre-1976 MAMS candidates. Out of a total of 77 candidates only 35 could appear for the Interview. The Interviews were conducted by the Fellows/Members of the Speciality Boards at the respective departments of the A.I.I.M.S., New Delhi. The examination in Preventive and Social Medicine was conducted in the Conference Hall of the National Medical Library, New Delhi. Vice-Presidents of the N.B.E. (except Dr. K.P. Bhargava) were present at the examinations. The examination was inspected by a team of 5 Inspectors from the M.C.I. The report of the Inspectors has been received. Government orders on the recommendations of the M.C.I. are awaited. Thirty-one candidates passed the examination.

August 1979 examination : The next MNAMS examinations (Theory) will be held on August 6 and 7, 1979. In all 926 candidates (736 for Primary and 190 for Final) have been registered for the August 1979 examinations. Applications for the subjects of Forensic Medicine and Nuclear Medicine have also been received and this will be the first examination to be conducted in these subjects.

Recognition of Institutions : The Medical Council of India has recognised 109 non-teaching Hospitals for purposes of training for the MNAMS examinations. All hospitals recognised for Housemanship/Diploma in Speciality are also recognised for purposes of MNAMS training. The M.C.I. has also agreed that candidates trained at Institutions abroad recognised by the respective speciality Board/University/Medical Council etc. will be accredited for purposes of MNAMS examinations.

Ann Natl Acad Med Sci (India), 15, 2, April-June 1979

Notes and News

Association of Radiation Oncologists of India : An Association of Radiation Oncologists of India has been formed to promote scientific development of the speciality and progress of radiotherapy in the country. The Association also aims at up-lifting the present status of personnel in this profession. Dr. A.D. Singh and Dr. T.K. Dutta have been elected President and Hony. General Secretary respectively of the Association which has its office at : Department of Radiotherapy, P.G.I M.E.R., Chandigarh.

Hundred Years of Malaria Research : An International Symposium **Hundred Years of Malaria Research** sponsored by the Indian National Science Academy, Indian Council of Medical Research, National Academy of Medical Sciences (India), Indian Statistical Institute, Dept. of Science and Technology (Govt. of India), and Dept. of Health and Family Welfare, Govt. of West Bengal, will be held during January 17-19, 1980 at the Institute of Postgraduate Medical Education and Research, Calcutta. Scientists and research workers, directly or indirectly, involved in any facet of the problem of malaria are cordially invited to register their names for participation in the symposium by writing to :

Professor K.P. Sengupta
Convenor,
International Symposium : Hundred Years of Malaria Research,
Institute of Postgraduate Medical Education and Research,
244, Acharya J.C. Bose Road,
Calcutta-700020.

10th International Conference on Health Education : The 10th International Conference on Health Education will be held at London on 2-7 September, 1979. Details can be had from : The Conference Centre, 43 Charles Street, Mayfair, London W1X 7PB, England.

ICMR Awards

Basanti Devi Amir Chand Prize : The Basanti Devi Amir Chand Prize for the year 1979 has been awarded to Dr. S. Kameswaran, FAMS, Director, Institute of Otorhinolaryngology, Madras Medical College, Madras, for his outstanding contributions in the field of noise pollution in South India and its effects on population and measures to abate the same.

Dr. P.N. Raju Oration Award : The Dr. P.N. Raju Oration award for 1978 has been presented to Dr. Vinodini Reddy, Deputy Director, National Institute of Nutrition, Hyderabad, for her outstanding work on vitamin A deficiency in children.

Raja Ravi Sher Singh of Kalsia Memorial Award : The Raja Ravi Sher Singh of Kalsia Memorial award for 1978 has been presented to Dr. Pradeep Seth, Assistant Professor, Dept. of Microbiology, A.I.I.M.S., New Delhi, for his outstanding work on herpes simplex virus and cancer cervix.

Sandoz Oration Award : The Sandoz Oration award for the year 1978 has been presented to Dr. B.P. Gothoskar, Scientist Incharge, Division of Biophysics, Cancer Research Institute, Tata Memorial Centre, Bombay, for his outstanding contributions in immunology of chronic myeloid leukemia.

Dr. Y.S. Narayana Rao Oration Award : The Dr. Y.S. Narayana Rao Oration award for 1978 has been presented to Dr. Raj Narain, FAMS, Ex-Project Director, Tuberculosis Prevention Trial, Madras, for his outstanding contributions in the field of tuberculosis prevention.

Dr. V.N. Patwardhan Prize : The Dr. V.N. Patwardhan award for 1978 has been presented to Dr. K.A.V.R. Krishnamachari, Assistant Director, National Institute of Nutrition, Hyderabad, for his outstanding contributions in the field of food and environmental toxins.

Dr. Kamala Menon Medical Research Award : The Dr. Kamala Menon Medical Research award for 1978 has been presented to Dr. P.M. Udani, FAMS, Ex-Director/Professor, Institute of Child Health, Grant Medical College, Bombay, for his studies on tuberculosis of children with special reference to tuberculosis of the central nervous system.

Dr. M K. Seshadri Prize : The Dr. M.K. Seshadri Prize and medal for the year 1978 have been presented to Dr. Shanti Ghosh, FAMS, Ex-Head of the Department of Paediatrics, Safdarjung Hospital, New Delhi, for her outstanding contribution in community medicine.

M.N. Sen Oration Award : The M.N. Sen Oration Award for 1978 has been presented to Dr. K.S. Chugh, Prof. and Head, Department of Nephrology, Postgraduate Instt. of Medical Education and Research, Chandigarh, for his outstanding contribution to the study of etiopathogenesis and management of acute renal failure.

Kshanika Oration Award : The Kshanika Oration Award for 1978 has been presented to Dr. Maharani Chakrabarti, Reader, Department of Biochemistry, Institute of Medical Sciences, Banaras Hindu University, Varanasi, for her outstanding work on the molecular basis of host-virus interaction.

Shakuntala Amir Chand Prize : The Shakuntala Amir Chand Prize for the year 1978 has been awarded to Dr. S.K. Bhattacharya, Reader in the Department of Pharmacology, Institute of Medical Sciences, Banaras Hindu University, for his outstanding research contribution in neuropharmacology.

The Shakuntala Amir Chand Prize for 1978 has also been awarded to Dr. P. Bhaskaram, Senior Research Officer, National Institute of Nutrition, Hyderabad, for her outstanding contribution to studies on nutrition and immunity.

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NATIONAL ACADEMY OF MEDICAL SCIENCES (INDIA)
C-II/16, Ansari Nagar, New Delhi-110016

NOTICE

The National Academy of Medical Sciences (India) will award the following Medals/Prizes during the year 1979-80 :

1. **Dr. S.S. Misra Memorial Award :** Through the courtesy of late Dr. S.S. Misra, a Founder Fellow of the Academy, Dr. S.S. Misra Memorial Bronze Medal plus cash prize will be awarded for the best unpublished work in any field of bio medicine by a young bio-medical scientist (below 40 years). Papers submitted by other scientists who are not considered worthy of Bronze Medal plus cash prize may be awarded Certificates of Merit by the Academy.

2. **Sir Shriram Memorial Award :** Through the courtesy of Shriram Foundation, the Academy will award Sir Shriram Bronze Medal plus cash prize to a bio-medical scientist for his/her best published paper during the preceding three years on Community Medicine (Community Health, Medical Education and Hospital Administration). The work should have been done in India by a bio-medical scientist of any age. The scrutiny of joint paper will only be done if the name of the first author of the joint paper is that of the cadidate applying for the award.

3. **Dr. R.M. Kasliwal Award :** Through the courtesy of Dr. R.M. Kasliwal, a Founder Fellow of the Academy, Dr. Kasliwal Prize/Medal will be awarded to the best worker in the field of 'COLON AND ITS DISEASES'. No restriction of age. The nominee will have to supply along with his/her paper, complete bibliography on this subject including work done in India.

4. **Dr. Vimla Virmani Award :** Through the courtesy of Dr. (Mrs.) Vimla Virmani, a Fellow of the Academy, Dr. Vimla Virmani Bronze Medal plus cash prize will be given to a bio-medical scientist below the age of 45 years for his/her best work in the field of "Rehabilitation of the Neurologically Handicapped patients based on published or unpublished work with particular emphasis on the applicability of the work of the Socio-cultural and economic considerations prevalent to the Indian community/communities".

Conditions

I. The scientist should not have received any prize for the same paper (s) in the past.

II. Four copies of each paper should reach the office of the Academy latest by the 30th September, 1979. These should be accompanied by a forwarding letter giving a brief bio-data of the scientist along with the title of Medal/Prize for which the paper/nomination is submitted.

III. Selected papers for Dr. S.S. Misra Memorial Bronze Medal/Certificates of Merit and unpublished papers for Dr. Vimla Virmani Award will be published in the Annals of the National Academy of Medical Sciences.

IV. Scientist selected for medal/prize or certificate or merit will be invited at the cost of the Academy to present their papers at the annual meeting of the Academy in January/Feb. 1980.

V. The awards will be formally presented at the time of the Convocation of the Academy on the next day of the presentation of paper.

Ann Natl Acad Med Sci (India) 15, 2, April - June 1979

YEAR BOOK

Of The

NATIONAL ACADEMY OF MEDICAL SCIENCES (India)

1978

(Supplementary)

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*Retiring in 1979.

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6.	Dr. K.N. Rao	Member Secretary

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10.	Dr. C. Gopalan D.G., ICMR, New Delhi.	Member
11.	Prof. Satish Chandra, Chairman, U.G.C.	Member
12.	Dr. A.K.N. Sinha, Representative from I.M.A.	Member
13.	President, I.A.A.M.E.	Member
14.	Dr. K.N. Rao	Member-Secretary

15th Convocation

The 15th Convocation of the National Academy of Medical Sciences (India) was held on Jan. 7, 1978 at the Rajendra Memorial Research Institute of Medical Sciences, Patna.

Shri J.N. Kaushal, Governor of Bihar, delivered the Convocation Address.

Number of Fellows/Members who have resigned/expired since inception

Number of Honorary Fellows lost by death since inception (7+1)	8
Number of Fellows lost by death since inception (56+4)	60
Number of Members lost by death since inception	5
Number of Fellows resigned since inception	3
Number of Members resigned since inception	2

Number of Fellows and Members on roll at the end of 1978

Hony. Fellows	Fellows	Members
8	321	410

Fellows Elected in 1978

ANTIA, FRAMROZ PIROJSHAW, B.SC., M.B.B.S., M.D., M.S, (Illinois), F.R.C.P. (Lond.).

b. August 10, 1916. Hon. Physician and Gastroenterologist, Tata Memorial Hospital, Bombay - 400012; Consulting Physician, Radiation Medicine Centre, Bhabha Atomic Research Centre, Tata Memorial Hospital, Bombay - 400012; Emeritus Hon. Professor of Gastroenterology and Medicine, B.Y.L. Nair Hosp. and T.N. Medical College, Bombay - 400008; Consultant Gastroenterologist, Jerbai Wadia Hospital for Children, Bombay - 400012; and Consulting Physician, B.D. Petit Parsee General Hospital, Bombay - 400036; Res. : 534, Sandhurst Bridge, Bombay - 400007.

BHALERAO, RAJARAM AMRUT, M.B.B.S., M.S., F.R.C.S. (Ed.).

b. April 11, 1933. Prof. & Head of Dept. of General Surgery, Seth G.S. Medical College & K.E.M. Hospital, Bombay - 400012. Res. : 144 A, Naraya Sadan, V.P. Road, Bombay - 400004.

BHARGAVA, PUSHPA MITTRA, B.Sc., M.Sc., Ph.D.,

b. February 22, 1928. Head, Centre for Cellular and Molecular Biology, Regional Research Laboratory, Hyderabad - 500009.

CHUGH, KIRPAL SINGH, M.B.B.S., M.D., F.I.C.A. (USA).

b. December 12, 1932. Professor of Nephrology, Postgraduate Institute of Medical Education & Research, Chandigarh - 160012. Res. : House No. 58, Sector-24, Chandigarh.

DANDIYA, PREM CHANDRA, B. Pharm., M. Pharm., M.Sc. (Toronto), Ph.D. (Toronto).

b. September 5, 1926. Faculty of Medicine, Al Fateh Univ., Post Box No. 13628, Tripoli, Libya. Res. : SB - 37, Bhawani Singh Road, Jaipur - 302004.

DASS, ANUSUYA, M.B.B.S., M.R.C.O.G., F.R.C.O.G.

b. August 8, 1918. Hony. Consultant, Railway Hospital and Tirath Ram Hospital, New Delhi. Res. : 126, Malcha Marg, Chanakya Puri, New Delhi-110021.

DHRUVA, ASHWINKUMAR J., M.B.B.S., D.A.

b. June 17, 1925. Prof. & Head of the Dept. of Anaesthesiology, Seth G.S. Medical College & K.E.M. Hospital, Parel, Bombay - 400012.

HASAN, MAHDI, M.B.B.S., M.S., (Hons.), Ph.D., F.R.M.S. (Engl.), F.I.C.S.

b. March 21, 1936. Prof. of Anatomy, Jawaharlal Nehru Medical College, Aligarh - 202001.

HIRANANDANI, LAKHUMAL HIRANAND, M.B.B.S., F.C.P.S. D.L.O. (Lond.), F.R.C.S. (Engl.).

b. September 17, 1917. Professor Emeritus & Adviser to Dept. of Otolaryngology and Head & Neck, B.Y.L. Nair Hospital & Topiwalla National Medical College; Hon. E.N.T. Surgeon, Bombay Hospital, Breach Candy Hospital, Jaslok Hospital. Res. : A 3, Amerchand Mansion, Opp. Cowasji Jehangir Hall, Next to Y.W.C.A., Madame Cama Road, Bombay - 400001.

MAHADEVAN, BHASKER, Maj. Genl., M. B. B. S., D. P. H.. D.T.M., & H., F.R.I.P.H.H., F.I.P.H.A., F.C.C.P.

b. January 13, 1916. Director of Rural Health Services and Training Programme, St. John's Medical College & Hospital, Bangalore - 560034. Res.: No. 187, Defence Colony, Indra Nagar, Bangalore - 560038.

PINTO, JOACHIM MATHIAS, M.B.B.S., D.M.R.D. (Lond.), F.R.C.R. (Lond.).

b. February 24, 1916. Head of the Depts. of Radio-therapy and Radio - Diagnosis, Tata Memorial Hospital, Parel, Bombay - 400012. Res. 134, Hill Road, Bandra, Bombay - 400050.

RAMAKRISHNAN, M.S,, M.B.B.S., M.S., F.A.C.S.

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Ann Natl Acad Med Sci (India), 16, 2, April-June 1980

Welcome address

By

Dr. Banwari Lall, FAMS
Honorary Secretary
National Academy of Medical Sciences (India), New Delhi

At the XVIIIth Convocation of the National Academy of Medical Sciences (India), at Jawaharlal Auditorium, A.I.I.M.S., New Delhi, on March 22, 1980.

Respected Uprasthrapati Ji, distinguished dignitaries, honoured guests, dear colleagues, friends, Ladies and Gentlemen :

I extend to you, on behalf of the National Academy of Medical Sciences (India) and on my own behalf, a very hearty and warm welcome to this our XVIII Convocation.

Established in 1961, Sir, the Academy has completed 19 years of its earthly existence. In human scale, the transition from teens to adulthood is a crucial phase and the ancient wisdom dictates that it is at this juncture, the threshold of adulthood, that some advice and proper guidance would benefit most.

Nobody would fit the role for this better than you, Sir. You have been a Jurist of world fame, a diplomat, and an eminent academician, a great teacher and writer and above all a great humanist. We consider ourselves singularly fortunate therefore, to have you amidst us at this prestigious function, and look forward to the words of wisdom from you. We are, indeed, very grateful, Sir, that in spite of your heavy and multifarious engagements, you accepted our request to be with us today.

To our distinguished guests, we are specially obliged that they could find time from their heavy and onerous engagements, all the more so, today being a working day, to join us on this important occasion.

Some of our Honorary Fellows, Founder Fellows and past Presidents are also present today. We are specially delighted to have them with us on this occasion.

It was the effort of about 100 Founder Fellows that brought the Academy into existence, with the foremost object of cultivation of scientific knowledge and its application to human welfare. Some of the founder members who are present here today, would be happy in the knowledge that, from a humble beginning, the Academy has found a significant place in the country's medical heirarchy and is now striving hard towards advancement of that objective. They might recall, perhaps, nostalgically, the First Convocation in 1963 addressed by no less a person than late Dr. Radhakrishnan, the then President of India. We joyfully welcome them.

We are particularly thankful to the Director (a distinguished Fellow of the Academy), the Dean and the senior Faculty Members of the All-India Institute of Medical Sciences, many of whom are also Fellows of the Academy, who, as in the past, came to our help and provided us all facilities to organise this important function. We are very grateful to them.

To the newly elected Fellows and Members, we extend our hearty congratulations for their success and welcome them to our fraternity. Their presence will add strength and meaning to our endeavours.

Sir, there are a large number of colleagues, staff members and friends present today, who gave their best, unreservedly without expectation of any award or even an individual mention. As the first designated Secretary of the Academy, I say that we are very appreciative of their efforts and offer my thanks to them individually and collectively.

And then, there are those who are often forgotten or missed inadvertantly in any welcoming or thanksgiving speech. I would, therefore, ask their forgiveness for any lapse on our part and hope they will accept our thanks all the same.

Once again, we take pleasure in welcoming you one and all. Thank you.

Ann Natl Acad Med Sci (India), 16, 2, April-June 1980

Presidential address

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At the XVIIIth Convocation of the National Academy of Medical Sciences (India), at Jawaharlal Auditorium, A.I.I.M.S., New Delhi, on March 22, 1980

Uprashtrapati ji, Fellows and Members of the Academy, Distinguished Guests, Ladies and Gentlemen :

We are most obliged to you, Uprashtrapatiji, and feel greatly honoured for your very kindly sparing your most valuable time to be with us today and offer us your advice and words of wisdom. Our newly elected Fellows and Members will cherish this opportunity to receive their scrolls from you. I am also most happy to associate myself with the welcome given to all of you present here today by the Secretary on behalf of the Academy. We further very much appreciate the presence with us of some of our distinguished Honorary Fellows and past Presidents of the Academy, to share with us a certain sense of achievement at the measure of success attained by the National Academy of Medical Sciences and the National Board of Examinations during the past year. With a certain sense of pride I have to report to you that Dr. K.L. Wig, our Founder Fellow and past President and Dr. Gunaratne, our Honorary Fellow have only few days back been honoured by being awarded the D.Sc. degree—Honoris Causa—by the Banaras Hindu University. Many other Fellows and Members of the Academy have also received quite a few prestigious awards and honours. In the recently given B.C. Roy Memorial awards there were 5 Fellows and Members of the Academy amongst the awardees. Thanks to the help, support and guidance received from the Fellows and the Members, the Academy and the National Board has been able to achieve some of its objectives. Credit for this progress is due to all of you—the Fellows and Members of the Academy, and the large number of other professionals associated with the activities of the National Board of Examinations—who have jointly given their best for helping in the various activities undertaken by our organisations.

As most of you are aware, in this Academy we take pride in the fact that the two landmarks in its development have been associated with the names of two of our most revered and illustrious national leaders. The Academy was inaugurated in 1961 by Pt. Jawaharlal Nehru, whose vision and unstinted support for the development of Science and Techonolgy in every field, helped us to establish this Academy on a proper footing. We are further proud of the fact that in 1975 our reverred Prime Minister, Smt. Indira Gandhi—who also happens to be one of our most distinguished Honorary Fellows—considered our Academy worthy of being given the responsibility of conducting the affairs and duties of the National Board of Examinations, which has since been conducting national level postgraduate examinations in the various specialities of medicine. We hope that in carrying out our academic and other functions, we are coming up to the expectations of our leaders who placed their trust and faith in us.

Our efforts in various fields have to a great measure succeeded, thanks to the generous and continuing support received by us from the Ministry of Health and Family Welfare, and we wish to convey our sincere thanks to the Ministers of Health, the Secretary of Ministry of Health and all his colleagues, and the Director General of the Health Services Dr. B. Sankaran and all his colleagues, who have been taking personal interest in enabling us to carry out our legitimate activities and functions. We are most happy that one of our senior Fellows occupies the exalted office of the Director General of Health Services which is a very good augury for the Academy.

Although the Academy started functioning with a Memorandum of Association signed by 8 Fellows, keeping in view that one of the important objectives of the Academy was the recognition and encouragement of merit in all branches of medical sciences, 100 medical scientists from all over the country were elected as Founder Fellows in the year 1961. Since then the Academy has been giving recognition to personal merit by electing eminent professionals belonging to various branches of medical sciences as its Fellows. Our toal Fellowship strength by now has gone up to 367. I further feel most happy to inform you that with the election to Fellowships during this year, the Fellowship of the Academy has become fully representative of the country as a whole, as it will now have Fellows on its rolls who belong to all the regions and States of our country.

The Academy has also been playing its due role in trying to achieve its other important objectives of promotion of knowledge of medical sciences and its practical application to problems of national welfare, through the holding of scientific sessions, orations, group discussions, etc, and through the setting up of some committees for offering advice in particular areas and fields. In these efforts we have tried to coordinate with other medical and scientific academies, societies, associations, and institutions, as well as some of the Government and official agencies.

On the advice of a Working Group in 1975 the Government of India decided to set up a National Board of Examinations, for conducting postgraduate examinations at national level of high academic standards, with a view to the raising of standards of medical education in general and making available prestigious qualifications within the country and thus minimising the tendency to go abroad to acquire such degrees. This responsibility was given to our Academy, which has been trying to discharge its due role through a National Board of Examinations. The candidates who pass in its examinations are awarded the Membership of the National Academy of Medical Sciences. With a certain sense of pride we report the exceptional rate of progress achieved by this Board in the very short span of 4 years. Not only has this Board been able to set up 43 different Speciality Boards for holding postgraduate examinations in as many specialities of medical sciences, a total of 3090 candidates have already appeared in the various biannually held examinations held up to last year. Out of these nearly 1500 candidates have already cleared the Primary examination and over 200 have passed the final examination as well. Their numbers have been progressively increasing showing the popularity of such examinations, with over 1000 appearing in the examinations in 1979 alone, and 99 having cleared the Final examination during last year, who are being awarded Memberships today. A further demonstration of the popularity of these examinations is provided by the fact that the candidates appearing in these examinations have been the graduates of almost all the medical colleges in India. The Board has also been able to attract senior medical experts from all the States of the country to act as its examiners, and the examinations are being simultaneously conducted at over 20 different centres, including one in London, U.K. and another one in Australia for the benefit of Indian doctors working in those countries. It is further proposed to start an examination centre in U.S.A.

We must record our grateful appreciation of the help received from the Medical Council of India—especially from its President Dr. B.N. Sinha—as the Council under his dynamic leadership after its decision to recognise the MNAMS as equivalent to the highest postgraduate degrees, has given us all the help and support, which greatly helped us to achieve the present level of popularity and success. We look forward to further fruitful collaboration with the Medical Council and are assured of their fullest support throughout the tenure of the Presidentship of Dr. Sinha, who also is a senior Fellow and Council member of our Academy.

After taking over the added responsibilities of conducting such specialist examinations, the Academy has felt that it should also undertake certian training programmes. Some training programmes have already been initiated through the Chapters of the Academy in some of the major cities of the country, and I am glad to report that the response from the Medical Faculties at these Centres for organising and participating in these courses is most enthusiastic. In these efforts, in addition to our Fellows and Members, we are receiving full support from the medical institutions and the Specialist Associations, for which we are most thankful. A Committee is working out the Academy's programme for "Continuing Education" to be undertaken on the countrywide basis. We will be holding a discussion session on this today afternoon, and we feel happy and obliged that Dr. V.T.H. Gunaratne, Regional Director of World Health Organisation, who has wide experience, maturity and abiding interest in this is going to address this session and inaugurate it.

Another important objective for the Academy is to undertake work of national and international importance which the Academy may be called upon to perform by the public and the Government. With the acceptance of the Alma Ata Declaration and the Government of India's sincere efforts for achieving health for all by the year 2000, the development and training of appropriate health manpower in adequate numbers at all levels of the health professions, has assumed great importance and urgency. The Academy has offered its services to the Government for helping in these efforts and a Manpower Development Committee of the Academy has prepared a project programme which we will be soon forwarding to the Government.

A full report on the activities of the Academy and the National Board during the last year has been prepared by the respective Secretaries. In my brief report I have only tried to highlight some of our relevant and important activities.

Before I end this report, I must acknowledge with sincere thanks the role and support of Fellows and Members in general, and Members of the Council of the Academy and of the National Board of Examinations in particular, in achieving our objectives. Our special thanks are however due to Dr. K.N. Rao, Dr. N. Jungalwalla, and Dr. B. Lall, who in the capacities of Honorary Secretaries, have put in yoemans service for achieving these objectives. The measure of success achieved by us during this year as being reported by me is mostly due to their hard work and selfless service. In this they have been ably supported by their colleagues.

Although drawing justifiable satisfaction form our achievements, we are conscious of the fact that much needs still to be done, and that the Academy has a vital role to play, not only for the recognition, betterment and promotion of the medical profession, but also in helping to provide a high quality medical and health care delivery to the people. We have optimism that with the continued support from all of you, we will be able to discharge our legitimate functions to the satisfaction of everyone. Thank you.

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Convocation address

By

Shri M. Hidayatullah, Vice-President of India,

At the occasion of the Convocation of the National Academy of Medical Sciences (India) in the Conference Hall of the All-India Institute of Medical Sciences, on 22nd March, 1980 at 12.30 afternoon

President Dr. Anand, Fellows and Members of the National Academy of Medical Sciences, Ladies and Gentlemen :

I am very grateful to you and feel honoured to have been invited to be the Chief Guest at the XVIII Convocation of the National Academy of Medical Sciences and to insigniate certain Fellows and Members.

It is a unique occasion for the prize winners and awardees and I congratulate them whole-heartedly on their achievement. I must say that I owe an apology to you, Mr. President, for having put you out twice for this Convocation—firstly, I had to request you to shift the time of the Convocation from 4 p.m. to 11·00 a.m. as I have to preside over the Lecture by Lord F. Broackway in the afternoon today; secondly before I could come for your function, I had to be present at the Command Investiture Ceremony at the Rashtrapati Bhavan this morning, as a result of which I was late by half an hour, for which again you have my sincere apology. It is due to the fact that I do not have much free time of my own and have to attend certain things which are obligatory.

I am very glad, indeed, that the National Academy of Medical Sciences over the space of 18 years has made such a great headway. I must say I was a little puzzled when I received an invitation, because in this very Hall, I attended the Convocation of the All-India Institute of Medical Sciences a few days back. I, therefore, read through all the literature that you sent me to find out where this Academy fits in and after making full research in this behalf and learnt that after electing 100 Founder Fellows you have been electing more Fellows whose number reached the figure of 317 in recent years. With the addition of 50 newly elected, I find that the Fellwship now stands at 367. Well, it seems quite an achievement, because the Academy has been able to honour so many persons. Its functions correspond to the functions of the Royal Colleges of Physicians and Surgeons. The Academy can legitimately take pride in having established an institution equal to any in Britain or Edinburgh, and that our Fellowships and Memberships of the Academy are now being recognised all over the world.

As announced by the President in his introductory lecture, I have been invited to say a few words of advice. I am very sorry that I have not prepared any written speech. So I will go on with whatever I can say impromptu on this occasion. You must forgive me if it may be a little discursive and lacking in depth, although, I feel I am consuming much more time than I should. As far as advice is concerned, I think a doctor or a professional, who has practised in the field of Medicine and Surgery for quite some time and has then obtained Fellowship/Membership of the Academy, must be knowing his or her duties towards the patients, towards himself/herself, and towards the country. The trouble is that our country is not yet fully mature to receive such eminent doctors, partly because of poverty of the people and partly because of the facilities which they seem to lack. It is alright in a hospital, or inside an Academy like this, or an institution of the standing of All-India Institute of Medical Sciences, to provide all the necessary assistance and facilities to the sick, but outside in the country, it is very difficult for you to provide all such facilities to the common man. These are the practical difficulties faced during every day of our life. I am again repeating the pessimistic picture which I painted at the time of the Convocation of the All-India Institute of Medical Sciences. The two main troubles in our country are (1) the high cost of treatment because of the fees of the doctors, and (2) the cost of drugs involved in the treatment. It has been said by a wit that it is surprising that for the same disease the doctor cures a poor patient sooner than a rich patient. That is because more fees are involved in the latter case. It is also said that the potency of the drug is its price. When the patient knows the price his urge to get well is stronger because he knows that the next doses will cost as much as the first dose. Therefore, it is the cost of treatment as a whole which is the deciding factor in our life. Many of us cannot afford to go in for costly drugs to cure ourselves. Therefore, we have to submit ourselves to our fate. I would, therefore, implore the doctors, Fellows and Members of the Academy, to be a little generous towards the poorer sections of our community.

After a long time—25 years to be exact—I entered the profession of Law and found that many of my clients could not afford to pay my fees and to such of them I gave my legal advice free.

Quite often, we just follow the directions of the doctors. I am reminded of a writer who in her book "Doctors and Dietician" describes how she consulted experts—she was over-weight. When she went to a doctor, the doctor was asked what was necessary for her diet and he gave her a list saying that those were the things she should take and those were the things which she should not. They were fats, carbohydrates, minerals etc. All the things prescribed for her she found were present in chocolate eclairs, which she very much relished and she kept on taking chocolate eclairs only. She continued to put on weight but could not understand why. So you see how a doctor's advice is something wrongly understood.

I do not wish to hold you any longer and wish to conclude my address by again extending my congratulations to the recipients of Membership and Fellowship this morning from the President of the Academy. Thank you.

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Inaugural address

By

Dr. V.T.H. Gunaratne,
Regional Director,
World Health Organization, Regional Office for South-East Asia, New Delhi.

At the Session on Continuing Education, held during the Annual Convocation of the National Academy of Medical Sciences (India), New Delhi, on March 22, 1980

President of the National Academy of Medical Sciences, Dr. B.K. Anand, Ladies and Gentlemen,

It gives me pleasure to welcome the distinguished members and guests to this session on continuing education. I am particularly happy that the Academy has felt the need to devote its energies to continuing education and that it has started organizing courses at the various Chapters all over the country.

This need has also been recognized in WHO. The World Health Assembly passed two resolutions, one in 1971 and the other in 1974, calling upon the Director-General to assist in the development of continuing education programmes for health personnel in various countries.

Continuing education for the health professions has also been a subject of concern for the countries of this region. At the thirty-second session of the WHO Regional Committee for South-East Asia, which was held in New Delhi in September last, a number of delegates brought it up during the discussions and urged WHO to assist in the organization of continuing education programmes in the countries of the Region. These discussions centered, to a considerable extent, on how the provision of continuing education could and should be directly geared towards the promotion of "Health for all by the year 2000" within the framework indicated in the Alma-Ata Declaration, which is now accepted as a major social goal by all countries.

Historically, as far as the medical profession is concerned, continuing education is not a new idea in response to a newly recognized need. It had its origins in pre-Christian Greece, and both Aristotle and Plato used essential elements of continuing education in their teachings. The need for continuing education springs quite directly out of self-evident but basic truth—namely, that it is never possible for a medical doctor to acquire, in the course of his basic and post-basic training programmes, all the skills that will be needed for a lifetime of professional service. Life-long learning, which is continuing education in its broadest and truest sense, is a pre-requisite for life-long professional effectiveness.

While the need for continuing medical education is as old as the profession itself, the nature of the need and its importance have undergone refinement and change. Many basic forces have contributed, and will contribute, to the reshaping of this idea.

First, there is the increasingly rapid expansion of the boundaries of medical knowledge which, over the last thirty years, has resulted in the half-life of knowledge growing ever shorter. This has pointed up the need for regular continuing education if we are to keep up with the times.

Secondly, there is the increasing realization that many types of doctors are ill-trained to meet the pressing and urgent needs of primary health care, thus requiring massive investment in re-training programmes.

Thirdly, there is a clear need for doctors to work closely as members of an effective health team with other categories of health personnel. This requires planning, implementation and evaluation of well-conceived training programmes.

These aspects clearly bring out the very nature and purposes of continuing education. Continuing education does not consist of providing a few *ad hoc* refresher courses as money becomes available, in order that doctors, nurses, auxiliaries and other types of workers can update their knowledge and keep abreast of new developments and ideas. Continuing education does not only have an updating function, it also has a remedial function, that is, of overcoming the ill-effects of the irrelevance that characterizes many curricula (in all training programmes) in relation to health needs. It has, in addition, a catalytic function—that is, it can prepare personnel at all levels to deal effectively with newly emerging problems connected with (*i*) the adoption of newly available technologies for diagnosis and treatment at peripheral levels; (*ii*) the need to work effectively as members of a front-line health care team; (*iii*) the need to develop sensitivity and adapt the provision of medical care to the social values of the community, and (*iv*) the need to involve the community in the planning and provision of health care, and of the need to engage in "self-help". These ideas are all directly related to the quality of care that is provided, are all relatively new and therefore are unlikely to have been included in the basic training of currently practising health professionals. As a consequence, they constitute proper subject matters for continuing education programmes.

Ladies and gentlemen, what I am saying is that continuing education is not just a patchwork quilt consisting of a few courses. It is a broad programme of action, directed towards very important ends. It aims to : (1) help professionals keep in touch with practice more effectively; (2) help them overcome the irrelevant and deficient features of their basic training, and (3) expand the horizons of their professional competence by taking on new skills and competencies to deal with new problems.

The next point I wish to make is the need for careful planning for an effective continuing education programme.

An educational programme of merit and worth can only be expected to result if it is deliberately planned for. In our medical schools we recognize this by spending endless hours deliberating on the contents of the curriculum, the methods by which students are to be examined, and many other considerations. The same is, of course, true in those institutions which train nurses, physiotherapists, and various other categories of health workers. It appears to me that at the present time there is often not adequate careful planning or forethought in the sphere of continuing education, and I would like to suggest that we should adopt equally rigorous approaches to continuing education as we do in basic educational programmes. I should here like to raise a number of issues for your consideration.

It might seem superfluous to state that any educational programme needs clear-cut objectives. Continuing education programmes will derive direct benefit if they have well defined objectives and these purposes are clear to the students and to the teachers at the outset. Clear objectives for such an educational programme provide it with a sense of direction and go a long way towards ensuring that the efforts of teachers and students complement each other. Objectives should be formulated in such a way that they make learning an interesting and exciting task, and thus lead students to become motivated to life-long learning. One of the most effective ways of achieving this is to orient objectives as a whole towards problem-solving. It must also be remembered that it is only when a programme is based on clear-cut objectives or targets that it becomes possible to choose intelligently methods of evaluating the effectiveness of the programme.

Next, there is the question of choosing the most effective methods of teaching and learning; for example, if we have a programme whose principal overall objective is to assist the doctor "to work effectively as a member of a health care team in a primary health care situation", then we would be unlikely to help a group of doctors through a programme of lectures on the "theory of effective team work". You would need to help them to : (1) define what was meant by effective team work, and (2) place them in situations which fostered the development of these skills—and this might involve the use of such newer approaches to learning as "role playing", the "observation and critical analysis of people in real life situations", and the development of "micro-teaching programmes", which helped them to develop and refine their team-work skills. We would also have to take into consideration the learning habits and behaviour of adults, since experiments have shown that adult learners behave in very different ways from children and young persons. They have a greater background of professional experience, they wish to participate more actively in training programmes, and the "distance" between them and their teachers is much less. Continuing education programmes are therefore most unlikely to be effective unless the teaching methods are very carefully selected, and unless the methods of learning take into account the adult status of the learners. Effective educational programmes result from careful planning and not by accident.

We also need to think of the evaluation of continuing education programmes when they are being planned. Educational evaluation is frequently added to a programme as a mere afterthought. We hold a workshop, a conference, a seminar or a series of such, and we then assume that the participants will have derived some benefit. Rarely do we go further and ask such questions as : (*i*) what specific benefits were derived? (*ii*) did all individuals derive equal benefit—or did some do so more than others? and (*iii*) what specific benefits were derived—and more importantly, were they connected to the purposes of the educational programme? Many educational programmes remain unevaluated, and we cannot therefore say whether they have been effective or not.

I would like to mention one other aspect of continuing education, which is related to career opportunities and reward structures. Carefully planned programmes of continuing education should be considered an essential ingredient in the long-term planning of careers of groups of professionals, and of the individual doctor, nurse, or auxiliary. As these persons gain greater experience and seniority, then naturally they will be expected to take on greater and greater responsibility. Continuing education provides the natural, career-long vehicle for training people to take on these added (and changed) responsibilities.

There is, finally the question of resources and logistics in the planning of continuing education programmes. If we are to develop fully worked out plans for continuing education which make use of all opportunities, then we will need to provide adequate resources to meet the task. Courses will have to be arranged during periods which do not clash with participants' other responsibilities. It is also vitally important that these courses are not of too long a duration, otherwise they will weaken the provision of essential health services, which are already in short supply. We shall have to train the persons who are going to plan and provide the resources on which the programmes are based. We shall have to identify and arrange in order of priority those needs which are the most pressing and urgent. We shall have to marshal the necessary resources and budget so that programmes can be planned, implemented and thoroughly evaluated; and we shall need to evaluate these programmes in terms of whether they lead to qualitative improvement in all categories of health personnel, and whether in the end result they lead (in turn) to qualitative and quantitative improvements in health enjoyed by the people.

Ladies and gentlemen, I have, this afternoon, tried to share two basic ideas with you. First, that we need to expand our understanding of the nature and purposes of continuing education : it lies at the centre of professional competence, and is not an afterthought devoted to "helping people catch up with new knowledge". Secondly, that it will not occur unless it is methodically and rigorously planned for, unless it is equally rigorously evaluated for its impact and effectiveness, and unless we are prepared to allocate to it the resources that are needed.

I would like to congratulate the National Academy of Medical Sciences for having addressed itself to this important subject.

I wish you success in your endeavour. Your success will be my success because as an Honorary Fellow of your distinguished Academy, I feel privileged to be considered one of you.

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Dr. R.V. Rajam's 80th Birthday Memorial Oration—1979

*Whither health care for the millions

D. Jaganatha Reddy**

Vijaya Hospital, Madras

I am conscious of the honour done to me by the President and members of the Council of NAMS-India, in requesting me to deliver Dr. R.V. Rajam's 80th Birthday memorial oration of the National Academy of Medical Sciences at its Annual Convocation. I express my deep sense of gratitude to them. I am proud to have been assigned this task, as Dr. Rajam M.S., F.R.C.P., F.R.S., F.A.M.S., was my reverred teacher. He is an outstanding graduate of Madras' Medical College, bagging all the prizes and medals successively throughout the course. He is an eminent clinician, erudite scholar, distinguished teacher, internationally reputed researcher, has several original publications to his credit, illustrious past president of our National Academy, doyen of our profession, social scientist, and medical historian. He could take justifiable pride and credit for enhancing the stature of the departments of S.T.D. and the high quality and standard of work carried out in these areas as the Founder Director of the Institute of Venereology, Madras Medical College. Which ever position he occupied, he left the stamp of excellence and perfection and added lustre and dignity to that Institution. He is revered and greeted with warmth of affection all over the country by the public in general and members of our profession in particular. His captivating smile, convincing and persuasive conversation in gentle voice coupled with calm demeaneour account for his unparalleled achievements.

Being a social scientist deeply concerned with the health of the masses of the country, I have chosen the topic for the oration :

"Whither Health Care for the Millions"

chiefly to observe the reaction of all those concerned with health care of the people although may not be provocative enough.

Our foremost problem is population explosion. It was 361 millions in 1951 and is today 668 millions and will be 920-1000 million by the year 2000. Our National Population Policy in 1976 has done much to bring down the annual growth rate to 1·8 per cent but since a couple of years owing to lack of governmental drive, there is a trend to an annual addition of 13-14 millions. Although it is projected that birth rate

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*Dr. R.V. Rajam's 80th Birth day memorial oration (1979) delivered at the Annual Convocation of the National Academy of Medical Sciences (India) at New Delhi on 23-3-80.

**Director and Pathologist

would reach 30 per 1000 by 1980 and 25 per 1000 by 1982-84, with the resultant growth rate of 1·5 to 1·0 per cent a year, we are to implement vigourously integrated health programme covering Family Welfare, M.ch., immunisation and nutrition.

This has to be a crash programme. By persuasion and education small family norm be made acceptable by the masses.

It is heartening to observe that where literacy is high and the women are economically not dependent and are in a position to share with their male partner in decision making as is in Kerala there is an appreciable decline in birth rate and infant mortality (Tables III and IV). Chinese aim at zero population growth by 1990. By 2000 China's

Table I. Population trends 1950-2000.

Year	Population in millions	% increase per decade	Live births per 1000	Deaths per 1000	% annual growth rate
1951	361	13·81	40	15	2·5
1961	439	21·64	38	15	2·3
1971	548	24·8	37	15	2·2
1980	668		35	15	2·00
2000	920		28	14	1·4

Table. II. Population trends and economic state 1979.

Population in millions	Birth rate	Death rate	Annual % growth rate	Infant mortality rate	% of population under 15 years
660·9	34	15	1·9	122	41

Life expectancy in years	% Urban population	Per capita GNP	% Annual economic growth rate
50	21	$150	3·2 to 3·8

Table III. Comparative statement of vital statistics.

States	Birth rate			Death rate		
	Rural	Urban	Combined	Rural	Urban	Combined
India	34·2	27·8	32·9	16·0	9·4	14·7
Kerala	25·6	24·6	25·4	7·3	6·8	7·2
U.P.	32·3	41·5	40·3	21·7	11·9	19·1
Gujarat	37·8	31·8	36·1	16·8	11·0	15·3

Table IV. Comparative statement of infant mortality.

States	Rural	Urban	Combined
India	143	89	134
Kerala	57	47	54
U.P.	182	132	176
Gujarat	177	113	161

population will be 1200 millions. Present annual growth rate is 1·0 per cent and by concerted efforts will be reduced to 0·8 per cent next year and to 0·5 per cent by 1985. One child for each couple is propagated. This is done by patient presuasion and not by administrative machinery. Simple effective contraceptives are being ensured and are popularising birth control knowledge. Stress is made in the rural areas as 800 million Chinese live in villages. Approaches are different with varying groups. Unanimity among all political parties is an essential element for successful implementation of population control programmes—this as in China is greatly determined by the Political Philosophy. Involving community and opinion leaders to carry the torch of enlightenment into interior for the urgent need for small family norm, along with the easy availability in the proximity of the people, if need be domiciliary supplies of contraceptives be made; rural co-operatives be entrusted to distribute the contraceptives at low or no cost.

Third world population is disproportionately large forming two thirds of the world's total population (Table V).

Health scene of the country is far from satisfactory. Sixty per cent of the people are under-nourished or suffer from malnutrition, Forty eight per cent of the rural people and 41 per cent of the urban folk are below the proverty line. Two hundred million adults are unlettered.

We need to be serious about implementing the proposed strategy to arrest population growth in the 1978-83 draft plan document which by 1982-83 will bring down birth rate to 30 per 1000 : This could be achieved by protecting 36 per cent of reproductive age group couples by 1983. (Table VI).

During the Fifth Five Year Plan we fell short of achieving the targets listed (1974-78) (Table VII).

Only 25 per cent under immunisation and 50 per cent under prophylaxis listed could be implemented. Migration of population from villages to towns has created urban ugliness eroding into the meagre water and sewerage facilities and largely contributing to the rapid increase in slum zones. All these have laid pressure and strain on the limited welfare resources. Only 20 per cent of the rural people have migrated to towns

Table V. Comparative statement of population of developed and developing countries.

Countries	Population in Billions	
	1975	2000
Developed countries	1·1	1·3
Developing countries	2·9	3·9
World's total	4·0	5·0

Table VI. Proposed family planning measures 1978-83.

	Sterilisations	IUDS	CC *&* op users	Total
In millions	25	5	·25	55

Table VII. Fifth five year plan achievements under family planning.

	In millions	
	Target set	Achieved
Sterilisations	18·00	13·00
IUDs	5·9	2·10
CC users	8·8	3·0
Couples protected	4·2	2·5

in China, greatly due to the better living conditions and opportunities for employment provided. To a great extent morbidity and mortality could be dramatically reduced if preventive care to all communities is assured. This covers the provision of safe drinking water, proper disposal of solid human waste (adequate sewerage system) better housing, total coverage of children and expectant mothers by immunoprophylaxis and the vigorous spraying of DDT to erradicate malaria. Improvement of environmental sanitation be given top priority although it is difficult to take it to remote and scattered villages. Recrudescence of malaria is a great threat. 3·2 million cases of leprosy, tuberculosis continues to inflict a heavy morbidity and 1·5 per cent of the people are infected and there are half a million of open cases, 136 million are susceptible to filaria, of which 85 million reside in the villages, infectious hepatitis, dysenteries, diarrhoeas, enteric fever, tetanus, whooping cough and diphtheria and some of the more important infectious diseases that need immediate attention for erradication.

Since independence there has been tremendous awareness and concern both by the goverment and the policy makers to improve the health of the people. Basing on the Bhore Committee (1946) and Health Survey Planning Committee Reports (1961) planning to provide the requisite health man power was undertaken. Today there are 112 medical colleges with annual student admissions over 13,000. In USA there are 100 medical schools admitting 9000 and U.K. is considering to increase to 4000-6000 students a year. USA has been flexible in its admission requirement during the seventies, even taking Ph. D's offering a 3 year MD course and limiting the teaching hospital bed strength and facilities to a minimum by taking advantage of neighbourhood community hospitals for clinical instruction with the object of providing a bias towards primary care—community medicine; sometimes ignoring university requirements and in a way loosely getting affiliated to the university. This is to reduce the number of immigrant health personnel.

Table VIII. Physician—population ratio, per 100,000.

USA	UK	USSR	China	India	Bangla Desh	Sri Lanka
183	169	185	*280	20	10	63

*includes bare foot doctors and midlevel workers.

We have 200,000 doctors, qualified in modern medicine, excluding those of indigenous systems of medicine. There is one doctor for 4000, one nurse for 8000 and one midwife for 20,000 people. Some places there is not a physician for 40,000 population. Our bed strength remains at 0·4 to 0·5 per 1000 population. Although over 10,000 physicians qualify each year, owing to maldistribution, rural sector avails only 30 per cent of the health care personnel. Owing to reluctance of the medical graduates to serve in villages and semi urban areas, there is increasing unemployment to the extent of 13,885 doctors, resulting in annual migration of 1000 doctors and sizeable number of nurses to USA, UK and middle east countries. Our western model of medical education and training is suited to export market and not far indigenous consumption. We need more nurses, laboratory technicians, radiographers, dentists, sanitarians/enviromental improvement personnel and pharmacists. USA has during the seventies adopted Nurse Practitioners and Physician Assistants for Primary Health Care assignments. A recent evaluation of their work compares favourably with those of primary care physicians. USA has also introduced another innovative measure by which 3550 MDs of internal Medicine are undergoing Residency Programme in community Medicine/Family practice (generalists) diverting the traffic to subspecialities under internal Medicine.

More interesting and spectacular is the manner in which China during the last 3 decades has been able to provide comprehensive community integrated primary health care to its now 1000 million, of which 800 million reside in villages. This covers availability of a doctor, safe protected drinking water, imporved environmental sanitation and sewerage system, total coverage of immuno-prophylaxis and attention to nutrition of children and expectant mothers. This has been possible due to their political, social and economic policies. China rapidly increased the output of existing medical schools, five fold increase of graduates and continues to grow faster than the output of universities. Embarked on "To mass" produce other kinds of physician like health professionals and assign them the title of "doctor". Restructuring of the course content to suit to meet the health care needs of the community and innovative experiments in medical education be the order of the day irrespective of the global context of standards. In this AIIMS has made a beginning.

Table IX. Physicians and mid level health practitioners in some countries, per 100,000 population.

	China	UK	USA
Mid level practitioners	—	25	6
Intermediate level phsicians	45	—	—
Bare foot doctors	200	—	—
Western type medical graduates	35	116	177

High cost of training western type of physician and the difficulty to maintaining them in rural areas, Chinese government decided to alleviate the shortage of physicians by faster and less costly means. As a result, lower priority was placed on the training of western type of physicians and a higher priority was put on the rapid expansion of less costly and more easily deployed intermediate level physicians and bare foot doctors. Each type of doctor regardless of the level of training is able to serve independently as the first contact physician treating self limiting illnesses, providing simple emergency care, family planning, counselling, immunisations and prescribing drugs. China's lack of independent universities, professional licensure, accreditation, peer review and malpractice legislation has made these policies easy to implement. Most impressive is China's success in bringing basic health services to rural areas and lower income urban neighbourhood. Low cost primary services are available six days a week, often on evenings and holidays—in schools, factories, day centres, government buildings and isolated villages.

During the post independent era there has been impressive yet irrelevant expansion of specialities and much money has been spent in establishing speciality Institutes. Race for specialisation even by the graduate who got the last rank after taking double the number of years to qualify, is the order of the day. This has resulted in the congregation of doctors in and around the medical colleges, in the cities and larger towns and reluctant to serve in rural and semi urban areas. This is for the consumption for the elite and provide opportunities of employment for the planners offsprings. Realising this the strategy during the Fifth Five Year Plan and draft plan for 1978-83 of the planing commission and the central government is to restrict admissions to medical colleges, not to open new medical colleges and to promote research relevant to the country. Priority is to provide health care and medical services to the rural areas and urban poor. Government of India accepting the recommendations of the Srivastava

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Committe's report (1976) for every 1000 of the population a voluntary community health worker and a trained dai will be provided. Male and female multipurpose health workers working at the subcentres or mini health centres of Tamil Nadu and Primary Health Centres will attend to integrated eradication programmes of malaria, filaria, tuberculosis, leprosy, STD *etc.* as also will assist in improving environmental sanitation. In addition to the existing 5250 PHC's 33000 sub centres (for every 5000 population one sub centre) 58 mobile health units and 14 mobile hospitals and a number of units for eradication of infectious diseases, 101 PHC's, 1293 rural hospitals and 33000 subcentres will be set up. Four hundred of the PHC's are to be upgraded to house 30 beds with referal services—serving as the primary referal centre. Tehsil and district hospitals will be expanded and provided with specialists to serve as secondary care/referal service centre and teaching and speciality hospitals are to provide tertiary care—three tire system of medical care. Each community block will be served by a PHC and one sub centre for every 5000 people. While according high priority to family welfare and planning strategy is to integrate MCH and nutrition programmes at all levels. By 1977, 28 districts have come under this scheme, and voluntary community health and Multipurpose workers are being trained at the PHC's and other hospitals for 3 months in elements of health sciences, hygiene, treatment of infectious diseases, first aid, to enable to offer basic health care facility to every 1000 people and include knowledge of traditional systems current in the place. In this each medical college is to take the responsibilty of 3 community development blocks and provide health cover to the people through the three PHC's Students will visit the centres during their course and Internees will work for 6 months in PHC or peripheral hospitals.

Recently I was greatly impressed by the activities of the Rural Health Centre of Christian Medical College, Vellore (CHAD) with its primary and secondary service units. Eighty female voluntary community health workers are providing primary care for 80,000 people in 80 villages and a mobile unit with a public health nurse and an Internee undertake immunisations and health check and prescribe drugs during their weekly visit. Commitment and dedication of the staff of the CMC at all levels to this adventure is worth emulating. This is illustrious example of medical college extension service-neighbourhood health care. Simllar health and Community Development Programme covers 21 villages with 70,000 people by Arogyavaram Development Society, Madonopalle.

Only 64000 villages enjoy safe drinking water. There are 1·52 lakh villages under the category of problem villages and during 1978-83 it is hoped at least a third of them will be given protected water supply. Twenty per cent of urban population in 1229 towns out of 3119 towns do not have protected water supply. Two hundred and seventeen towns have sewerage facility most of which is partial, covering 34 per cent of urban population. Urban ugliness and pollution due to lack of proper solid waste disposal threatens health of the people (Table X).

We are aware of the interests and inclinations of World Health Organisation and noteworthy action taken by Dr. H. Mahler in 1975 at the World Health Assembly in resolving to support primary health care and basic health services that all echelons of health services should support the needs of their peripheral activities and low cost drugs and vaccines developed. Our government is signatory to concepts and principles of comprehensive primary health care enunciated by WHO Conference on Primary Health Care held at Alma Ata in September 1978. The main tenet of this is the attainment by all peoples of the world by the year 2000 of a level of health will permit them to lead a socially and economically productive life. Robert McNamara while supporting the same posed the problem of how to tackle this gigantic task with diminishing resources, indicated World Bank's estimates of costs of services which are frightening though realistic.

1. To set up clinics and provide health workers to treat all ailments costs by 2000 year ($ 9 billions)—One community health worker/ANM for 1500 to 2000 people and one health facility for 8000 to 12000 people or every 10 km.

2. One health post with one vehicle per 1,000 people and training 125 ANMS and 250 CHW cost (or $ 5.00 per capita) exclusive of recurring cost on salaries drugs and supplies and maintenance ($ 2,500,000).

3. House to house spraying against malaria is $ 21.00 per capita annually.

4. Financial investment for providing good sanitation and clean safe water is enormous ($ 135 to $ 260 billions). By 2000 year will need construction of rural community stand pipe costs per capita ($ 20 to $ 26) and rural sanitation per capita ($ 4).

5. Cost of research funding of diseases in the developing world (1978): Malaria $ 15,000,000; Filariases $ 2,000,000 and Leprosy $ 2,000,000.

Water facilities provision in the house makes substantial difference to the incidence of disease in washing and sanitation from that of stand by pipe in the street to a reduction of 50 per cent of shigella diarrhoeas. Changing peoples habits in excretion and water usage takes more than introducing an adequate dependable and convenient new source. Makes no difference in the provision of tube wells as long as surface water is contaminated. Pervasive and effective health education campaign is required.

Fixed or mobile units be used for providing care package of nutrition supplementation, vaccinations (DPT and Polio) to children up to 3 years and child bearing mothers which can be modified as time demands.

In the 1978-83 draft plan a provision of 2095 and 2540 crores of rupees are allocated towards health, welfare and water supply respectively which is 5 per cent of the plan allocation of 69380 crores of rupees (Table XI).

We have from past experience seen that between allocation and achievement there is a widening gap, resulting in static unimproved health status of the people. Owing to distrust, desire to propogate political philosophy and an over riding ambition

Table X. Outlays for water supply and sewerage 1978-83 plan.

	Rs. in crores
Rural water supply	765
Urban water supply and sewerage	815
Total in crores	1580

Table XI. Plan allocation under social services 1978-83.

	Rs. in crores	%
Social services	9355	13·5
Education	1955	
Health and welfare	2095	3·0
Housing and urban development	2540	
Water supply	1580	
Social welfare and nutrition	305	
Backward classes and Harijan welfare	545	
Others—Rehabilitation, labour welfare etc	355	

Table XII. Defence expenditure of some countries (1975).

Country	Defence expenditure millions $	Per capita defence expenditure $	Per capita of GNP on defence %	% total Budget on defence
Soviet Union	103,800	409	10·6	—
USA	92,800	430	6·0	26·6
Peoples Republic of China	4,000 15,000	4-19	—	—
France	12,250	233	3·4	19·1
India	2,660	4	2·8	21·1

to acquire the status of supremacy over the nations, tensions have been built up during the last 3 decades between the nations. This has driven top thirty nations to allocate 325,884 million dollars towards defence in their 1975 budget, comprising 20 to 26·0 per cent of the budget (Table XII).

Quantity of explosives stored is 20 tonnes per woman, man and child in the world. Could this be avoided by mutual trust and understanding, so that this huge amount could be used for the promotion of human welfare activities that would ensure better health and living standards. Let us hope that nations gear their activities towards this noble goal.

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Achanta Lakshmipathi Oration—1979

*Neurohumoral correlates of behaviour

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During this century, man has achieved a marvellous control over his physical environment, but he has not yet learnt to live with his fellowmen in peace, amity and tolerance. In society there are different types of individuals, there are geniuses, there are criminals. Then this is the question—what is the basis of behaviour? Behaviour is the way living systems adjust to environment. Can endogenous chemical agents determine behavioural patterns? Only recently, physiology, biochemistry, pharmacology, neurology and psychiatry have begun to meet at the level of the nerve cell in an attempt to explore the mechanism of generation and transmission of nerve impulses.

In this era of stress and strain, tension hovers around the heads of millions of people like a vulture ready to swoop down on its victims at any time and in any place. Tension is the form of outward reaction to inner attitudes and manifests itself through the nervous system.

The word stress was used first by engineers. A stressor is an agent which disturbs equilibrium. The knowledge of stress in human subjects is due to the work of 3 pioneers. Cannon demonstrated the role of sympatho-adrenal system, typical of fight, fright and flight response. Selye showed the involvement of the pituitary-adrenocortical system. Psycho-endocrinologist Mason drew a line between the two systems. He emphasised the role of stress in leading to chronic diseases and showed that it is the emotional arousal that drives the neuroendocrine responses. Amygdala of the limbic system is involved in affiliative behaviour. Hippocampus provides sense of location in physical and social heirarchy.

Stimuli from various stressful situations are received by different centres in the brain through the sense organs. Depending on the severity, the entire brain, the autonomic and the peripheral nervous systems get involved. Stress acting through the pituitary and adrenal gland leads to systemic and metabolic changes in several organs (Fig. 1). Stressful situations can be created by self by recalling various pleasant and unpleasant past experiences and imagining catastrophic situations of future. Mental agitations occur repeatedly in one's life as a result of excessive love, hatred, jealousy, passion, anger *etc.*

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*Achanta Lakshmipathi Oration (1979) delivered at the Annual Convocation of the National Academy of Medical Sciences (India) at New Delhi on 23-3-1980.

**Professor and Head

The psychosocial stimulation resulting from the interaction in a susceptible individual with the environment triggers a chain of events that may eventually result either in psycho-somatic illnesses like hypertension, bronchial asthma, thyrotoxicosis or in behavioural disorders like depression, aggression, schizophrenia, epilepsy *etc.* (Fig 2).

Our studies have proved that biogenic amines are involved in the etiology of affective disorders (Sarada Subrahmanyam and Ramamurthi, 1979). Biogenic amines are biologically active substances derived from amino acids. An upset in the delicate balance between the different amines in the brain may cause behavioural changes. Rosenblat *et al.* (1969) were the first to suggest that changes in noradrenaline in the brain may be involved in depression.

The important biogenic amines are the catechol and indole amines. The main catecholamines are noradrenaline and dopamine and the indolamine, 5-hydroxy tryptamine. They are concentrated in the brain areas concerned with behaviour. They are produced both centrally and peripherally. Only small amounts of circulating hormones can enter the brain as they normally do not cross blood brain barrier. Their levels are affected by drugs which alter behavioural patterns.

Noradrenaline is synthesised from the amino acid tyrosine through the intermediates of DOPA and dopamine and its main end product of metabolism in the brain is 3-methoxy 4-hydroxy phenyl glycol (MHPG) and the principal peripheral metabolite is vanil mandelic acid (VMA). DA is metabolised into homo vanilic acid (HVA). Serotonin or 5-HT is synthesised from tryptophan and its major metabolite is 5-hydroxy indole acetic acid (5-HIAA). The changes in the brain chemistry are indirectly reflected in the CSF.

Material and Methods

In the present study an attempt is made to evaluate the role of biogenic amines in the etiology of affective disorders and the effects of different types of treatment on the amine levels.

The cases were selected from the Institute of Mental Health, Institute of Neurology, Voluntary Health Services Medical Centre and Dr. Boaz Rehabilitation Centre at Madras.

Normal subjects and patients without any neurological morbidity served as controls. Cases selected were schizophrenia, depression, aggression, epilepsy, mental retardation and drug addiction.

The main symptoms in schizophrenics were disturbances of sleep, negligence of personal hygeine, thought disorders and hallucination. Depression was characterised by extreme tiredness, getting odd feelings like jumping down from a height, seeing fantom figures and suicidal tendencies. In epilepsy there are recurrent and stereotyped

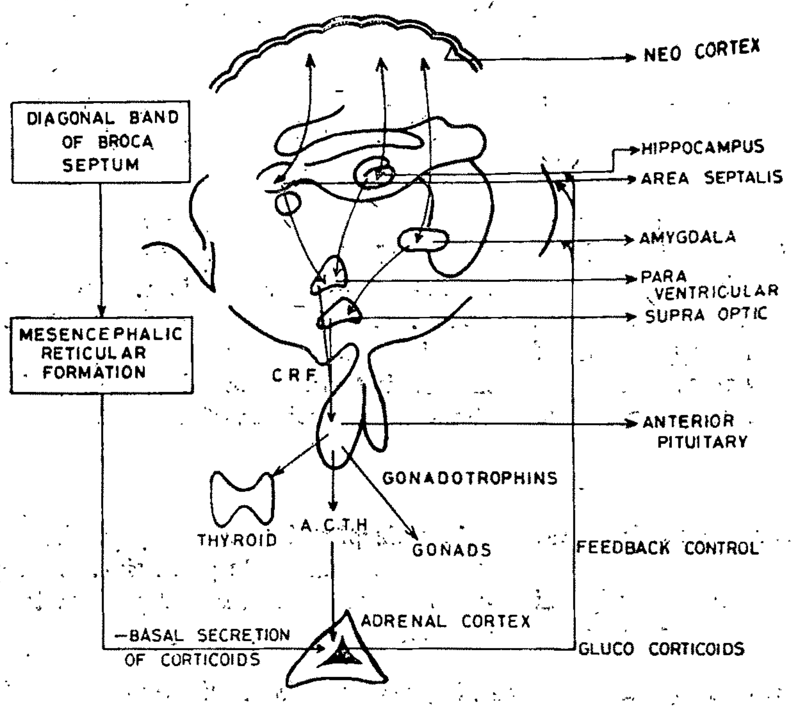

Fig. 1. Different areas of brain controlling secretions.

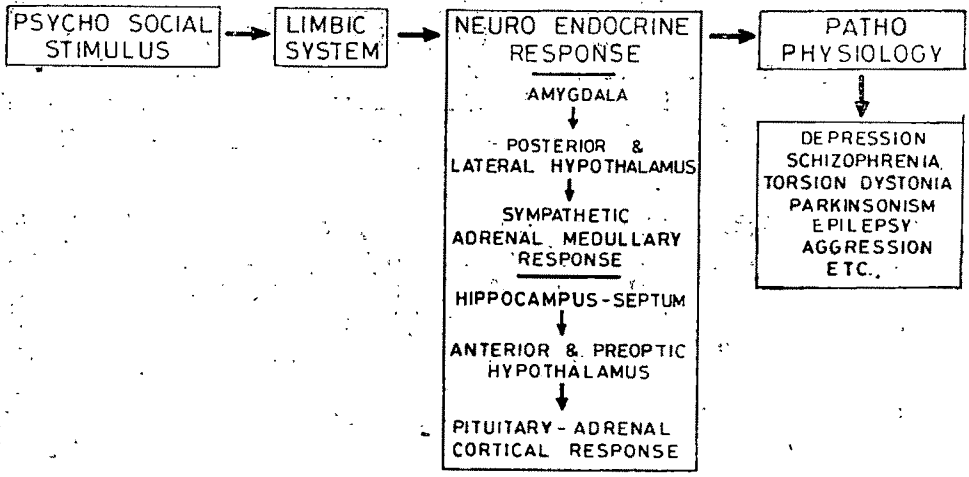

Fig. 2. Effect of psycho social stimulus on neuro endocrine response

manifestations of psycho sensory, psycho motor, autonomic and psychic phenomena on a background of disturbed consciousness. There was no constancy in the symptoms.

The aggressive patients had periodical outbursts of aggressive hyperkinetic behaviour and during the invervals they were almost normal, obedient, and amenable to reason. Only moderately mentally retarded subjects were included in this study.

The history of the drug addiction cases selected revealed that the main causes for addiction were diverse : (*a*) For ego satisfaction, (*b*) as a spirit of adventure, (*c*) to promote sales in case of company executives, and (*d*) adventitious. Most of them had a genuine desire to be free from addiction. The management of most cases was by psychiatric therapy. Some of the patients did not respond to psychiatric therapy. They had severe withdrawal symptoms and in them stereotaxic surgery which is only a phase in the management was undertaken (Balasubramaniam, 1972).

Treatment

1. Medical : The medical treatment in schizophrenia was a combination of electro convulsive and drug therapy by tranquilizers like chlorpromazine. In depression, tricylic antidepressant, imipramine was also administered. In epilepsy, eptoin, gardenal, tegratol, mysoline and calmpose were used.

L-tryptophan loading : L-Tryptophan 8 g/day orally in 3 divided doses for 2 months was administered in schizo-affectives and in chronic schizophrenics with and without chlorpromazine.

2. Surgical : Stereotaxic surgery was performed in refractory cases in all the groups. The surgical measures were basofrontal leucotomy in schizophrenia and depression where the higher functions were affected, amygdalotomy where there were aggressive symptoms, as in temporal lobe epilepsy, and aggressive hyperkinetic behaviour, and cingulumotomy where there was a drive or craving for drugs. Bilateral destructive lesions were produced at desired sites by injecting a mixture of wax, olive oil and myodil, the quantity varying from 0·5 to 0·8 ml. In some cases sequential surgery was performed.

3. Nonvolitional biofeed back : It is a technique by which a physiological function such as electrical activity of the brain is presented to a person usually in the form of visual or auditory signal. No active effort and co-operation from the subjects are needed. The alpha waves from the tempero occipital region were fed back to the patient in the form of light stimulus. The frequency of the flicker corresponded with the intensity of the alpha rhythm. This therapy was given in 5 schizophrenics, 6 depressives, 10 aggressives and in 6 epileptics. The monitor consists of an EEG amplifier and 4 active filters to split the waves into 4 different bands, delta (0·5-3·5 Hz), theta (4-7 Hz), alpha (8-13 Hz) and beta (14-30 Hz). The output of these filters was used selectively to excite the filament lamp (Fig. 3).

Biofeedback was given every day for about 20 minutes for a month, weekly once for 3 months and once a month for a further period of 3 months.

4. *Yoga and meditation* : Yoga and meditation are ancient scientific disciplines which coordinate different aspects of human personality—thus bringing about a state of equilibrium between mind and body. Six epileptic patients, 12 cases of mild aggressive hyperkinetic behaviour and 10 cases of mental retardation were taught meditation in two poses namely Vajrasana and Padmasana. They practised twice a day both in the morning and in the evening successfully for 6-9 months (Fig. 4).

Investigations

Investigations were carried out before and after treatment.

1. *Clinical :* Neurological examinations did not reveal any progressive dysfunction. The other systems were found to be normal.

2. *Psychological :* Assessments were done by Hamilton Rating Scale for depression, Wing's scale for schizophrenia, Minnesota multipassie personality test for epilepsy and Weschler's test for aggression.

3. *Biochemical :* In blood, in addition to the routine parameters plasma cortisol (Mattingly 1962) was estimated and in the CSF, MHPG, HVA and 5-HIAA (Korf *et al.* (1971).

In the urine VMA (Armstrong *et al,* 1957), MHPG (Ruthven and Sandler, 1965), HVA (Ruthven and Sandler, 1962), 5-HIAA (Subrahmanyam and Narayanan 1973) and 17-ketosteroids (Appleby *et al.* 1955) were assayed.

Results

In acute schizophrenia, both 5-HIAA and MHPG were reduced in CSF. With medical treatment the levels were increased. The same was the result with the surgical treatment. (Table I). In a few cases that were followed for 12-24 months it was found that the amine levels were almost restored to normal. In urine similar results were noted (Table II) (Subrahmanyam and Ramamurthy, 1979).

L-tryptophan loading in the schizo affectives showed an increase in 5-HIAA in CSF. One week after stopping the loading the level came down to pretreatment value. The psychological assessment (Hamilton rating scale) showed improvement in the affective symptoms. The level of 5-HIAA in CSF of chronic schizophrenics showed no significant rise after loading. The levels of MHPG and HVA showed no change in the CSF after loading in both groups. Similar were the results in urine in the groups studied. In schizo affectives tryptophan loading improved affective symptoms in 90 per cent of the cases. In chronic schizophrenics 75 per cent of the cases showed bizarre behaviour like restlessness, random movements, catatonia and increased hallucinations after loading. The group which received L-tryptophan along with chlorpromazine showed no change in the behaviour of the patients studied.

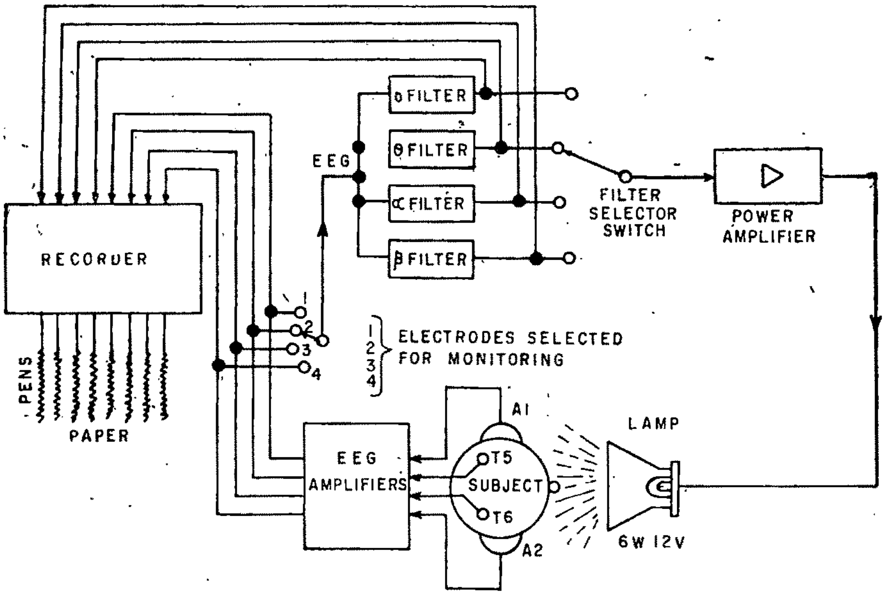

Fig. 3. Nonvolitional visual biofeed back system.

Fig. 4. Patients practising meditation

Table I. Lumber C.S.F. (ng/ml).

Group	No.	5-HIAA	MHPG	HVA
Normal	12	40·6±4·2	20·6±2·4	40·2±4·0
Control (with no neurological morbidity)	12	40·2±3·8	21·4±3·2	42·4±3·6
Acute schizophrenia	36	19·8±1·8	11·2±1·7	41·2±3·6
After medical treatment (3-12 months)	24	25·6±3·2	15·6±1·8	46·2±4·4
After medical treatment (12-24 months)	12	32·6±3·6	18·4±1·0	48·6±3·6
After basofrontal leucotomy	12	30·2±4·8	18·6±3·2	40·4±6·2
3-12 months	6	32·4±3·6	17·5±2·4	44·0±5·6
12-24 months	4	38·6±3·2	18·5±3·2	42·2±4·2

Table II. Urine (mg/day)

Group	No.	5-HIAA	MHPG	HVA	VMA
Normal	12	4·36±0·9	2·09±0·3	8·2±1·2	4·8±0·8
Control (without neurological morbidity)	12	4·0±0·4	2·09±0·2	7·8±0·8	4·4±0·6
Acute Schizophrenia	36	2·6±0·4	1·4±0·4	8·2±0·8	3·6±0·4
After medical treatment 3-12 months	24	3·8±0·8	1·4±0·3	2·2±1·1	3·8±0·3
After medical treatment 12-24 months	12	4·0±0·08	1·8±0·2	12·6±0·8	4·2±0·6
After basofrontal leucotmy	12	3·8±0·4	1·6±0·2	9·0±1·2	3·8±0·4
3-12 months after	6	4·2±1·0	1·5±0·3	9·6±1·3	4·0±0·6
12-24 months after	4	4·4±0·8	1·8±0·8	9·2±1·2	4·2±0·8

In schizophrenics who underwent biofeedback therapy, HVA level in CSF tended to fall after the treatment. No significant change in MHPG and 5-HIAA were observed. So also was the case with the urine.

Medical treatment was given in 20 cases of depression and in 10 cases basofrontal leucotomy was performed. Originally all of them had low 5-HIAA, MHPG and HVA levels. After medical treatment for a period of about 12 months, improvement in the amine levels was noted. Four days after the surgery there was an elevation of the amine levels.

The level of plasma cortisol was high in depressives and and there was a reversal of the diurnal rhythm. Cortisol in CSF was also high (Sarada Subrahmanyam *et al.*, 1979) (Fig. 5). The nonvolitional biofeedback showed that in depressive patients the levels of MHPG and 5-HIAA in CSF had a tendency to rise after treatment.

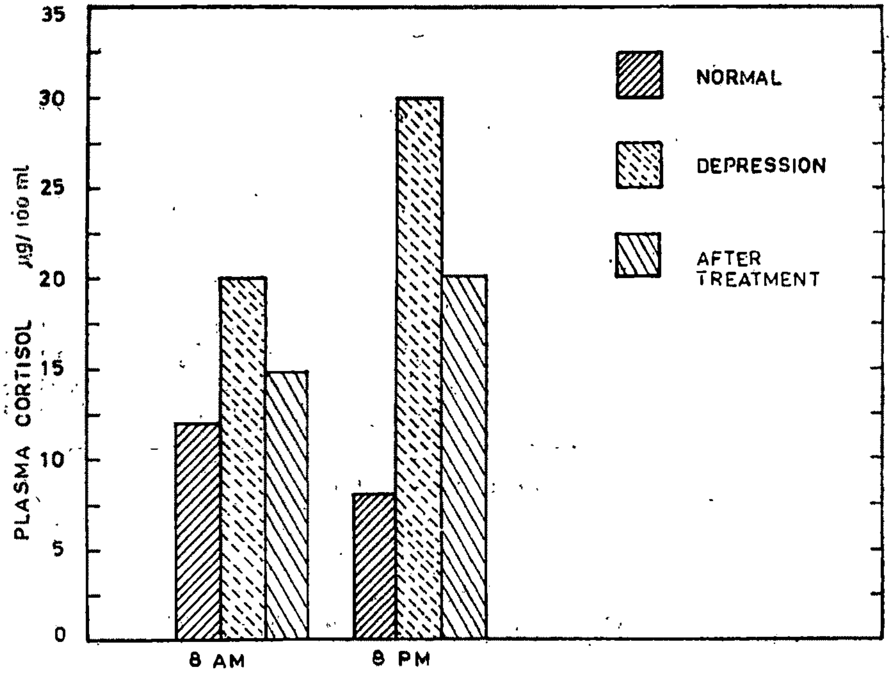

Fig. 5. Diurnal variation in plasma cortisol before and after treatment — one month.

In alcohol addicts 5-HIAA was low in CSF, HVA was normal and MHPG was raised. In morphine addicts the 5-HIAA was low and others were within normal range. In multiple addiction 5-HIAA was reduced and MHPG was higher. After cingulumotomy there was a tendency for the restoration of the normal levels (Table III).

Similar findings were noted in the urine in all the groups studied. There was definite clinical improvement in them and in most of them there was no craving for drugs. Few patients were followed up for more than 18 months (Table IV).

In temporal lobe epilepsy the level of 5-HIAA in CSF was initially low. After medical treatment for 12 months there was a slight increase. A rise towards normal was noted after amygdalotomy. The levels of MHPG and HVA were high initially, and after medical and surgical treatments the levels came down to almost normal values (Table V).

After nonvolitional biofeedback for 6 months the 5-HIAA levels in CSF showed a tendency to rise. No significant changes in the level of MHPG and HVA were noted (Fig. 6).

TM was practised by 6 epileptics. They initially had at least one attack a day. After 4 months, 2 patients became free from attacks and in the other four the attacks became less severe, and the interval between the attacks was prolonged. In CSF the levels of 5-HIAA showed a tendency to rise towards normal after treatment.

Table III. Lumber CSF (ng/ml).

Group	No.	5-HIAA	MHPG	HVA
Normal	12	40·6±4·2	20·6±2·4	40·2±4·0
Drug addiction				
(a) Alcohol	10	20·6±1·2	26·2±2·6	40·4±3·6
Immediate after cingulumotomy	6	30·2±2·6	17·2±2·4	38·2±2·8
3-18 months after	3	32·4±3·2	18·6±2·6	40·0±2·2
(b) Morphine	12	28·6±4·2	20·8±2·4	38·6±2·6
Immediate after cingulumotomy	10	32·6±3·8	20·2±1·6	38·6±3·2
3-18 months after	4	36·2±6·6	21·2±1·8	36·8±3·8
(c) Multiple	8	25·6±2·6	30·4±1·8	40·6±1·8
Immediate after cingulumotomy	6	33·8±4·2	19·2±1·4	38·6±1·6
3-18 months after	3	36·6±5·4	18·6±1·2	38·0±3·2

Table IV. Urine (mg/day)

Group	No.	5-HIAA	MHPG	HVA	VMA
Normal	12	4·36±0·9	2·09±0·3	8·2±1·2	4·8±0·8
Drug addiction					
(a) Alcohol	10	4·6±0·8	3·2±0·06	8·2±1·2	5·4±0·8
Immediate after cingulumotomy	6	3·8±0·6	1·8±0·2	7·0±0·6	4·6±0·6
3-18 months after	3	3·9±0·8	1·7±0·3	7·2±0·4	4·8±0·8
(b) Morphine	12	3·6±1·2	2·0±0·04	3·0±1·8	4·6±1·0
Immediate after cingulumotomy	10	4·8±1·2	1·8±0·06	7·6±1·2	4·2±0·8
3-18 months after	4	4·3±0·8	1·6±0·1	7·8±0·8	4·4±0·6
(c) Multiple	8	3·8±0·6	3·6±0·04	7·6±0·8	5·9±0·8
Immediate after cingulumotomy	6	4·0±0·4	2·7±0·08	7·6±0·8	3·6±0·6
3-18 months after	3	4·2±0·6	1·9±0·1	8·0±0·6	4·5±0·5

Table V. Lumber CSF (ng/ml)

Group	No.	5-HIAA	MHPG	HVA
Normal	12	40·6±4·2	20·6±2·4	40·2±4·0
Temporal lobe epilepsy	20	22·4±3·2	24·6±3·8	42·8±4·5
Medical treatment 12 months	9	28·6±4·0	20·2±2·8	43·6±3·0
After amygdalotomy	11	30·2±3·6	23·2±3·6	45·1±4·8
12 months after	6	28·4±2·2	22·4±2·8	42 6±4·2
12-24 months after	4	32·6±3·2	21·6±1·8	41·2±4·2

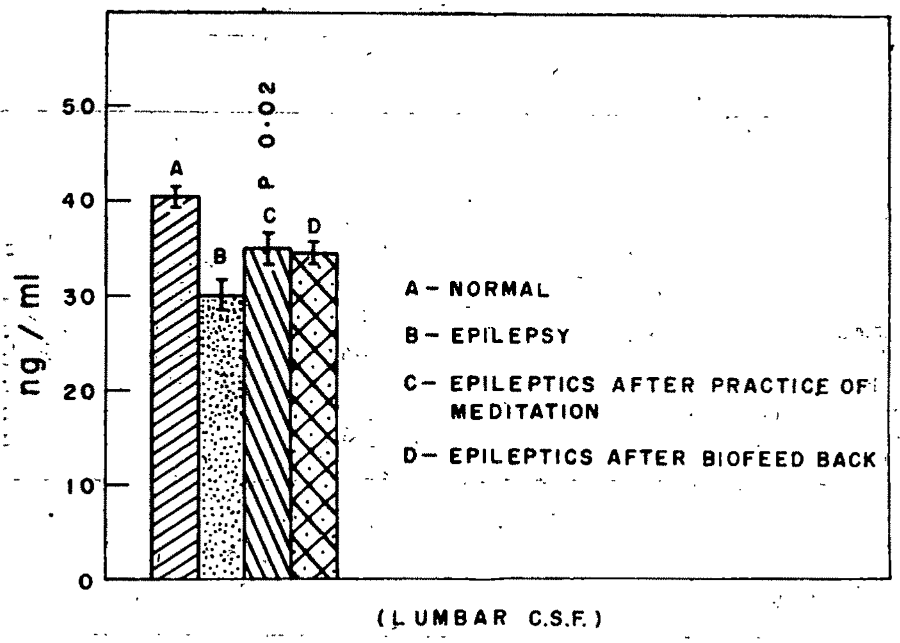

Fig. 6. 5-HIAA in C.S.F. before and after practice of meditation

The EEG pattern in epileptics who practiced meditation and underwent nonvolitional biofeedback showed an accentuation of alpha rhythm and the delta rhythm disappeared (Fig. 7).

In the first group of aggressive hyperkinetic behaviour, there were 20 cases, 16 of them were children. There was no significant change in the 5-HIAA levels in CSF but HVA and MHPG were increased. Bilateral amygdalotomy was performed in 14 cases and this served to reduce the levels of HVA and MHPG and the levels were maintained during the follow-up period of 24 months. The normal level was not reached at any time during the study (Table VI).

The same was the case with urine also. Clinically the few patients who turned up for the follow up studies were apparently normal although the patients became a little vegetative in nature.

In another group of mild aggressive hyperkinetic behaviour who practised meditation for 6 months, there was a significant reduction in MHPG and HVA levels in CSF which were initially high. Not much change was noted in 5-HIAA levels (Fig. 8).

Similar findings were noted in the urine also.

The plasma cortisol which was initially high showed a reduction after meditation (Fig. 9).

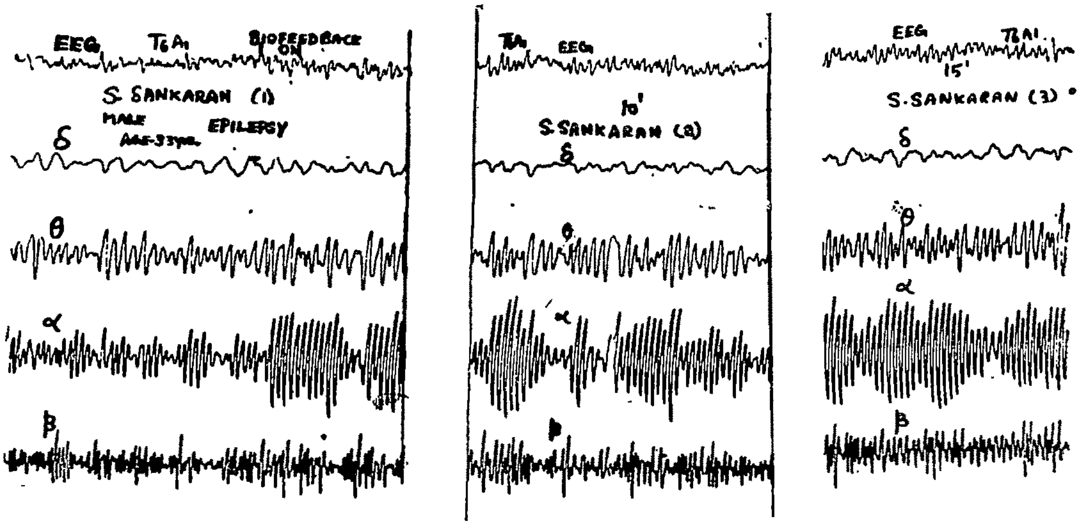

Fig. 7

Table VI. Lumber CSF (ng/ml)

Group	No.	5-HIAA	MHPG	HVA
Normal	12	40·6±4·2	20·6±2·4	40·2±4·0
Aggressive behaviour	20	43·4±4·2	36·4±3·2	56·0±2·6
After amygdalotomy	14	41·2±5·6	26·2±3·8	44·8±5·2
12 months later	6	40·6±4·2	25·2±4·4	46·3±4·2
24 months later	3	41·6±3·8	24·8±2·6	47·4±3·6

Nonvolitional biofeedback was tried in more severe cases and after treatment the levels of MHPG and HVA were almost restored to normal.

So also the plasma cortisol.

EEG studies after both meditation and nonvolitional biofeedback showed an augmentation of alpha rhythm and also the theta rhythm (Fig. 10).

In mental retardation levels of MHPG, HVA and 5-HIAA were initially lower than normal in the CSF. After practice of meditation the levels tended to rise. The urinary values of these metabolites showed similar results (Fig. 11).

The plasma cortisol also increased after the practice.

EEG studies revealed augmentation of alpha rhythm and enhancement of beta rhythm after the practice (Fig 12).

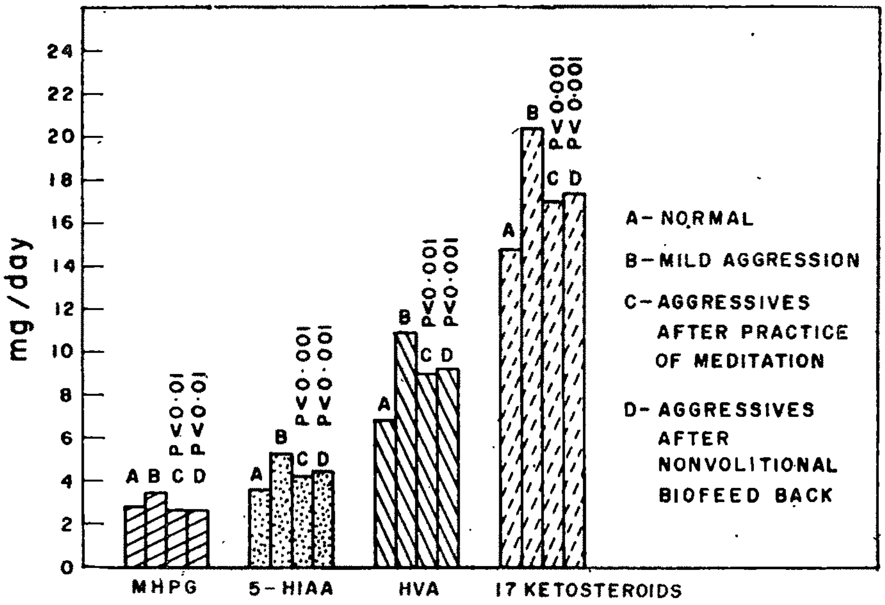

Fig. 8. Urinary excretion of metabolites of biogenic amines and 17 ketosteroids before and after meditation and biofeed back.

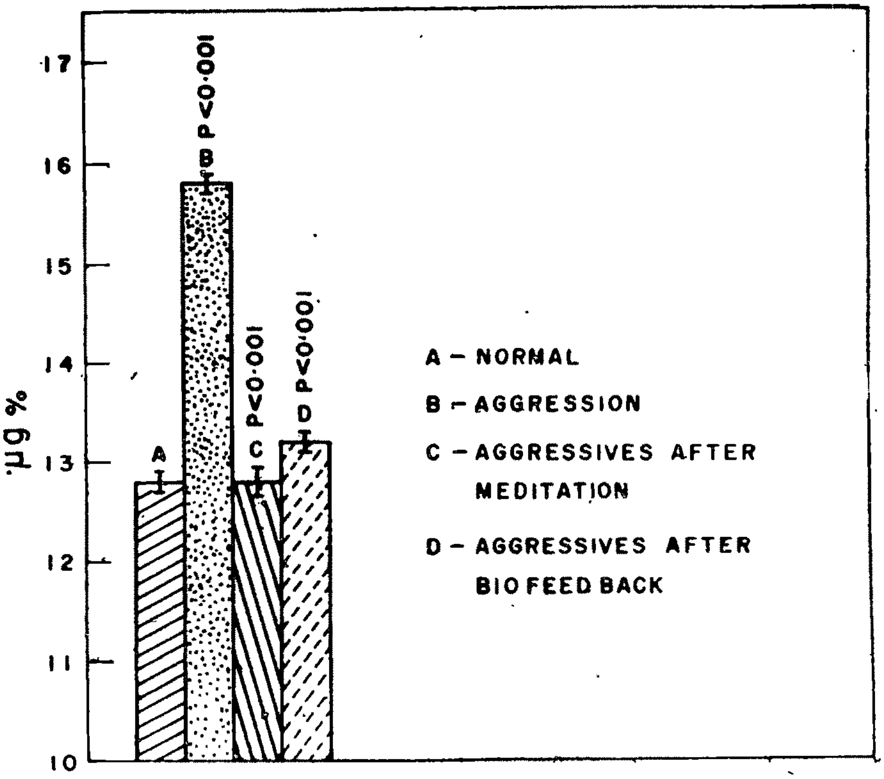

Fig. 9. Plasma cortisol in aggressives before and after meditation and biofeed back.

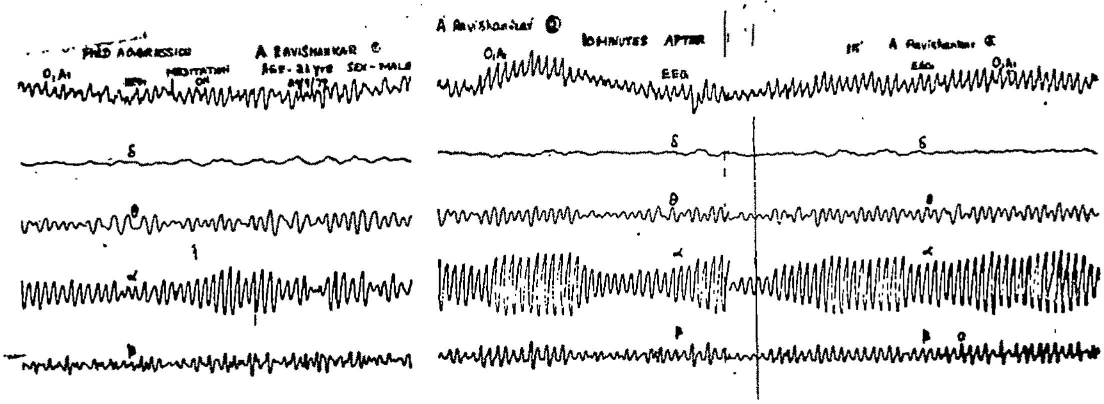

Fig. 10.

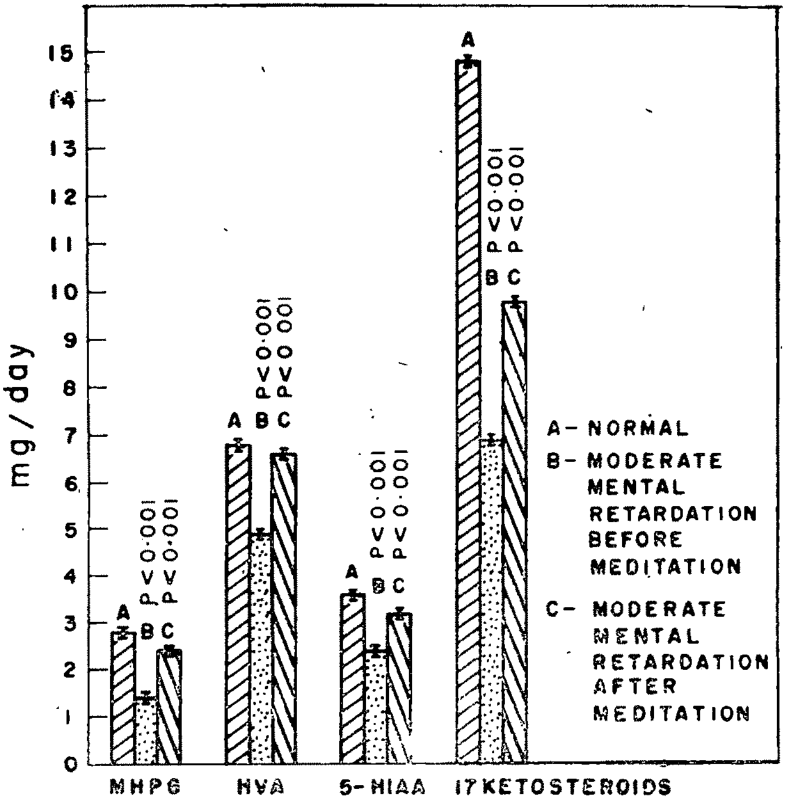

Fig. 11. Urinary excretion of metabolite of biogenic amines and 17-ketosteroids in moderate mental retardation.

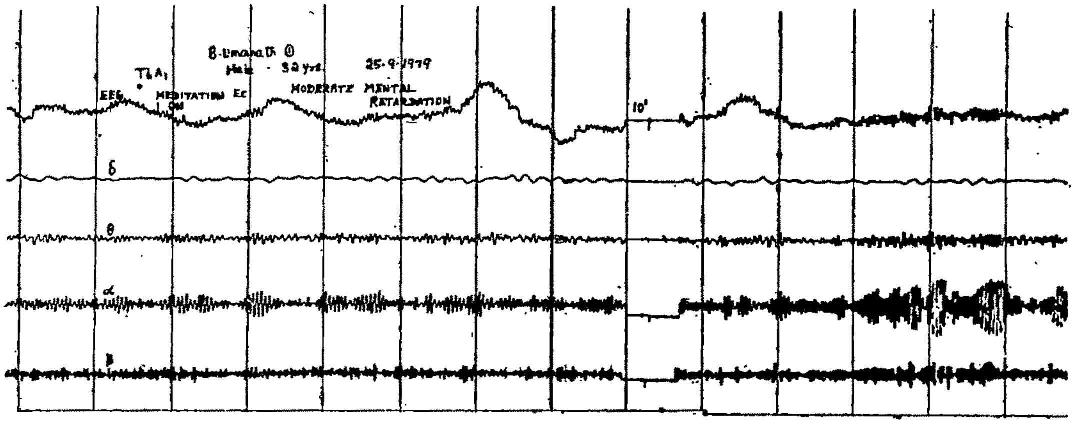

Fig. 12.

Discussion

The primary focus of interest in behavioural disorders is on the relative involvement of the brain noradrenergic and dopaminergic systems. The dopaminergic neurons are localised mainly in mesencephalon and median eminence. The cell bodies of noradrenergic neurons are situated in the lower brain stem and heavily innervate the stria terminalis—an area involved in affective aggression. Release of NA facilitates the affective aggression (Reis, 1972). Both NA and DA systems have connection with the central portion of amygdaloid nucleus. Increase in the exploratory behaviour and locomotor activity were noted with the infusion of noradrenaline into the cerebral ventricles (Segal and Mandel, 1970).

The high cortisol level in the aggressives and in depressives (Sarada Subrahmanyam *et al.*, 1979) indicate the intense psychotic turmoil in the brain due to the psychic trauma. After the meditation and biofeedback therapy the dopaminergic system gradually becomes resistant to the stressful effect of psychological stimuli, which through the hypothalamo-hypophysial adrenal axis decrease the adrenocortical stimulation. The reduction in cortisol level perhaps corrects the altered metabolism of noradrenaline and dopamine, thereby improving the behaviour.

Cerebellum normally sends inhibitory impulses to the cortex. When NA synthesis is increased it inhibits the cerebellum (Bloom, 1974) which in turn results in the release of cortex from the cerebellar control. This potentiates aggression and produces further increase in DA and NA.

The appearance of bizarre behaviour and increased hallucinations in chronic schizophrenics suggest that the administered tryptophan may have facilitated the formation of certain psychotogenic indolamines like DMT (dimethyl tryptamine).

The absence of any behavioural changes in schizophrenics receiving L-tryptophan along with chlorpromazine suggest that chlorpromazine has blocked the action of DMT.

The increase in the amine levels after practice of meditation in mentally retarded subjects may be correlated with the improvement in the behaviour (Sarada Subramanyam and Porkodi, 1980).

The accentuation of alpha waves during the practice of meditation may account for the tranquility and peace of mind experienced by the different groups of patients and also for relief of symptoms.

The probable mode of action of meditation and biofeedback may be :

1. The intensity of the psychic stimuli are reduced at the cortical level.
2. Unwanted extraneous stimuli from periphery undergo filtration and do not reach the cortex.
3. The reverberating vicious circle, cerebral cortex→limbic system→cerebellum→ cortex is broken thus bringing back normal behaviour (Sarada Subrahmanyam and Porkodi, 1980).

Conclusion

In conclusion it can only be postulated that biogenic amines play an important role in maintaining normal behaviour and there is a definite alteration in the metabolism of biogenic amines in behavioural disorders. The relative merits of different types of treatment were studied. Each one of them in different degrees served to correct the metabolism tending to restore the normal balance.

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Alpha fetoprotein*

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Introduction

Over the past ten years, there has been a growing interest in the study of special group of proteins associated with neoplasm—the onco-foetal proteins. The first and important member of this is alpha-feto-protein (AFP).

Alpha-feto-protein (AFP), an unique alpha-I-globulin makes its first appearance at the fourth week of gestation, then rises to a maximum level at about 12th to 13th weeks of gestation with a level of 3-4 mg/ml (Gitlin and Boesman, 1967). Afterwards, declines slowly reaching a level of 55 ng/litre at the time of birth and finally disappears from circulation in all but minute amounts within several days to 2-3 weeks after birth (full time delivery), with a half life of 3·5 days (Gitlin and Boesman, 1966).

Recently using radioimmunoassay, AFP has been detected in very small amounts in the serum of new born immediately after birth and also in the adult in the range between 1-16 ng/ml (Ruoslathi and Sappala, 1972*a*).

Before the introduction of radioimmunoassasy, AFP was thought to be present only in foetal serum and was therefore, referred as a foetal specific protein (fetoprotein). It was first detected in human foetal serum by Bergstrand and Czar, 1956.

Using immunofluorescence technique, AFP has been found to be synthesised principally by the human foetal liver but also by the yolk sac and gastrointestinal tract though at the time of birth, AFP is produced only by liver cells.

Two major hypotheses have been proposed regarding AFP synthesis in oncogenesis. In the first view, synthesis of AFP is being performed by a specialised cell of liver parenchyma (Hypothetical AFP forming cells) (Abelev, 1968). In the second view, AFP is produced by all hepatocytes at a certain stage of differentiation and not by mature hepatocytes which no longer produces AFP (Uriel, 1969).

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*A review paper

**Reader

Primary hepatocellular cancer

Tatarinov (1964) was the first person to detect the presence of AFP in the serum of patients with primary hepatocellular carcinoma (PHC). Subsequently, several studies from different geographical areas using gel diffusion technique, have confirmed the presence of AFP in the serum of patients with PHC (histologically proved) with an incidence varying between 40 to 80 per cent of cases (Abelev, 1971) though as low as 28 per cent (Alpert, 1969) to as high as 87 per cent (Kreshno *et al.*, 1970) has also been observed. Using radioimmunoassay, AFP has been detected in 86 per cent in PHC cases in almost all population studied (Shuster *et al.*, 1974).

To analyse the relationship of AFP in PHC, the sensitivity of technique used is very important as the serum concentrations of AFP is said to vary greatly. There is however, a suggestion of two different peak levels of serum AFP concentrations in hepatoma. One peak is in the range of 50 to 70 μg/ml and the other is in the range of 1 to 3 μg/ml (O'Conor *et al.*, 1970). Thus one can anticipate that in the latter group of cases, AFP will be negative in immuno-diffusion method. This has been bourne out in the studies where AFP were negative in immunodiffusion but had values above normal by radioimmunoassay (Waldman and McIntire, 1974).

Besides, various factors also affect serum AFP concentrations.

(*i*) A lower percentage of positive AFP sera has been observed in patients with PHC in U.S.A. and U.K. as compared to those in Africa, U.S.S.R. and Chinese groups (Abelev, 1971).

(*ii*) AFP is more positive in younger and male patients (Bagshawe and Parker, 1970) and less frequently in older and in female patients with PHC (Purves *et al.*, 1970).

(*iii*) Serum AFP is more related to the degree of differentiation of tumour (Abelev *et al.*, 1971). A negative (Alpert *et al.*, 1971*a*) or lower value (Purves *et al.*, 1970) has been noted in well differentiated tumours compared to positive or higher value in poorly differentiated tumours.

(*iv*) AFP has been found more often in those patients in whom PHC is associated with cirrhosis (Purves *et al.*, 1970). All these relationships have not been confirmed by O'Conor *et al.*, 1970.

(*v*) A definite correlation between the presence of AFP and Hepatitis B antigen in patients with PHC has not been confirmed (Masseyeff *et al.*, 1972) though the occurrence of the latter is often found (Vogel *et al.*, 1970).

(*vi*) With the growth of the tumour (PHC), AFP level in the patients sera generally increases but there is no correlation with the size and stage of tumoru (McIntire *et al.*, 1976). On the other hand, AFP level declined markedly or disappeared after radical resection of the tumour but reappears when hepatoma recurs (McIntire *et al.*, 1976).

Quantitative estimation of AFP have been tried as screening test for early diagnosis of PHC in high risk populations like Japan, China *etc.* but has found to be not rewarding because of negligible (Purves *et al.*, 1973) or small discovery (Hiral and Nishi, 1974).

However, quantitative assay of AFP have shown great promise towards evaluation of effectiveness following chemotherapy as favourable prognosis is indicated specially when there is a fall by more than 50 per cent along with persistence of decreased level for longer than 3 months (McIntire *et al.*, 1976).

Thus it would be reasonable to point out on the use of gell diffusion technique for detection of AFP in the diagnosis of PHC and radioimmunoasay to assess the course and response of the patients towards treatment.

The site of production of AFP in PHC is the tumour itself or by the patients' liver, synthesis of the later being somehow induced by the tumour process itself. Since AFP is not found in patients with Cholangiocarcinoma (Abelev *et al.*, 1967) while it is frequently present in hepatocellular carcinoma strongly suggests that it is the neoplastic hepatic parenchymal cells that are responsible for synthesis of AFP. This is further substantiated by immunofluorescence studies (Smith *et al.*, 1971) as well as tissue culture studies (Quelin *et al.*, 1972).

The reasons for AFP synthesis in PHC is obscure though two major hypotheses have been proposed. It is belived that AFP is produced in foetal liver cells and it disappears from the circulation when genes dictating its production are repressed at or around the time of birth. When hepatoma supervenes, cells dedifferentiate to a more totipotential state, these quiescent genes become derepressed and AFP production is again resumed (Uriel, 1969). Alternatively, the tumour arises from those cells which have the AFP genome in a nonrepressed form (Abelev, 1971).

Germ cell cancers

Besides primary liver carcinoma, germ cell tumour of the gonads is the other condition when AFP has been found to be positive in gell diffusion technique also. Initially, this was bourne out by Abelev *et al.* (1967) in 12 out of 24 cases. Subsequent studies have not only confirmed but noted its association with the gonadal and nongonadal germ cell tumours *e.g.*, testicular tumour (Masopust *et al.*, 1968), ovarian tumour (Masopust *et al.*, 1968), retroperitoneal tumour (Talerman and Haije, 1974), Presacral tumour (Roth and Panganiban, 1976) and anterior mediastinal tumour (Talerman and Haije, 1974).

The rate of occurrence of elevated serum AFP in these cases has been found to vary between 15 to 50 per cent (Talerman and Haije, 1974). Using radioimmunoassay, a higher percentage of positivity (71 per cent) is being observed (Waldman and McIntire, 1974).

AFP is said to be more detectable in serum when metastasis is widespread (Smith and O'Neill, 1971), when tumour is more malignant (Mawas *et al.*, 1969) and in children with these tumours than adults (Abelev, 1974).

The value of Serum AFP estimations in assessing the results of therapy, in patients with germ cell neoplasms has been carried out by a number of investigators. It has been emphasised that it is of value only when the elevated serum AFP level declines as a result of successful therapy as it indicates improvement but subsequent elevation points towards recurrence and a rising concentration nothing but a progression of the disease (Talerman and Haije, 1974).

The site of AFP synthesis in these patients is the tumour itself. Apart from the fact that normal yolk sac is one of the sites of AFP synthesis in the foetus (Gitlin *et al.*, 1972), demonstration of AFP in tissue sections by immunofluorescence (Teilum *et al.*, 1974) or in tissue culture studies (Kahan and Levine, 1971) or in extracts of tumour tissue (Wilkinson *et al.*, 1973) in gonadal embryonic carcinoma cases supports the contention. This is further being supported by the presence of yolk sac element in some germ cell tumours as well as detection of AFP in serum in yolk sac tumours (Wilkinson *et al.*, 1973).

Apart from yolk sac, Terato-carcinomas are capable of forming dedifferentiated tissue like hepatocytes, having the potentialities to produce AFP (Berry *et al.*, 1969) and the fact that cells of malignant undifferentiated embryonic tumours may produce specific substances acting as inducers or derepressors which are capable of restoring synthesis of AFP by liver cells, yet synthesis of AFP by yolk sac tissue seems to be the more likely explanation (Berry *et al.*, 1969).

Entodermal tumours

Using gell diffusion technique, AFP has been reported on rare occasion in the serum of patients with tumours of entodermal origin.

The primary tumours in all the patients have been reported either in gastrointestinal tract or in organs derived from the primitive foregut. In the former group, the primary tumour has been in the stomach mainly (Kozower *et al.*, 1971) or with metastasis to the liver and in rare exceptions like squamous cell carcinoma from the oesophagus (Spragins *et al.*, 1972). Of the foregut derivatives, pancreas (Andrieu *et al.*, 1974), lungs (Carling and Tompkins, 1972), gall bladder (Ishii, 1973) have been reported as sites of primary lesion.

However, the occurrence of elevated AFP serum concentration in association with metastatic involvement of the liver from various location is a rare event (Abelev, 1971). Using radioimmunoassay technique this association has been found to be more frequent *e.g.* 7 per cent (Alpert *et al.*, 1971*b*) or 13 per cent (Abelev *et al.*, 1971) in patients with hepatic metastasis from entodermal cancers.

The elevation of AFP in serum could be either due to increased synthesis of AFP in rapidly regenerating hepatic tissue adjacent to the metastasis or metastatic tumour foci itself is responsible for the production of AFP is not clearly known (Shuster *et al.*, 1974). However, the greater feasibility lies with the later concept because in patients with GI tract tumours, the appearence of AFP may reflect the latent capacity of such tissue to produce AFP since foetal gut has been shown to have low rate of AFP synthesis (Gitlin *et al.*, 1972). This is being further supported by a case in which AFP synthesis has been demonstrated both in primary gastric carcinoma and in hepatic metastasis (Kozower *et al.*, 1971).

Other liver diseases

It is true that serum AFP levels serve as a sensitive indicator of tumour activity but rarely it may also be positive in non-neoplastic hepatic disorders even in gell diffusion technique (McIntire *et al.*, 1976).

Such an observation was first noted by Alpert *et al.* (1968) in a single case in each of viral hepatitis and cirrhosis cases. Subsequently, Geffroy *et al.* (1970) reported presence of AFP in a case with hepatitis. However, Buffe and Rimbant (1973) reported high incidence of AFP (33 per cent) in children with acute hepatitis.

On the other hand, using radioimmunoassay, AFP have been found to be positive in viral hepatitis cases from 16 per cent to 52 per cent of cases (Hirai *et al.*, 1972; Shuster *et al.*, 1974). The value ranged from 65 to 440 ng/ml. Besides, viral hepatitis, AFP has been found in post necrotic cirrhosis (24 per cent), laennecs cirrhosis (15 per cent), chronic active hepatitis (32 per cent), with values over 40 but less than 3000 ng/ml (Shuster *et al.*, 1974, Waldman and McIntire, 1974). The occurrence of AFP in cases of hepatitis in children slightly weakens the value of this test for the diagnosis of hepatocellular carcinoma but elevation of serum AFP in hepatocellular carcinoma is usually more pronounced and persistent than that following viral hepatitis where it is low and transient in large number of patients (Masopust *et al.*, 1968).

It has been suggested that the rise in AFP is related to the amount of paranchymal damage since greater frequency is found in subacute necrosis (Bloomer *et al.*, 1974 and 1975). On the other hand, AFP concentration is increased as the transminase level returned to normal suggesting that AFP production occurs during regeneration of hepatocytes (Ruoslahti and Seppala, 1972*b*).

Increased synthesis might then be due to retrodifferentiation of mature liver cells during regeneration to a stage at which AFP is again produced (Abelev, 1971). Alternatively, it may follow proliferation or activation of those relatively undifferentiated hepatocytes that have AFP genome in a non-repressed state (Abelev, 1971; Ruoslahti and Seppala, 1972*b*).

In contrast with the frequent appearence of AFP in the sera of patient's with viral hepatitis, the demonstration of AFP in cirrhosis is unusual and less marked in conventional methods (Massin Kevitch, 1972). To explain the absence of AFP in cirrhosis and its presence in hepatitis, both being attained by regeneration of liver, it has been suggested that a definite minimal regeneration is necessary for AFP induction to occur and secondly the ability to synthesise AFP may become exhausted during long lasting regeneration or successive cycles of regeneration (Abelev, 1971). Using radioimmunoassay technique, Hirai *et al.* (1972) noted that 47 per cent patients with liver cirrhosis had elevated AFP.

The finding of elevated AFP in the sera of cirrhotic patients should however, alert one to the presence of a hepatoma. A primary difference in this connection may be that serum levels of AFP increase over a short period of time as compared to that cirrhosis where it usually decrease as the regeneration sub-sides.

The picture is quite different in Indian childhood cirrhosis where AFP has been observed in (45 per cent) patients in conventional technique (Nayak *et al.*, 1970). Probably, the failure of the normal transformation of foetal hepatocytes to adult type may account for AFP synthesis.

AFP has also been found in the serum of infants with congenital biliary atresia and neonatal hepatitis (Kang *et al.*, 1972). In addition to the mechanisms operating in acute viral hepatitis, the other cause may be persisting jaundice retarding the differentiation of foetal and neonatal hepatocytes leading to continued synthesis of AFP or viral infection, if considered as causative factor, may be responsible for derepressing the AFP genome (Kang *et al.*, 1972).

There are two other conditions where AFP have been demonstrated in the serum. One is hereditary tyrosinosis (Buffe, 1973). The cause is not known. The other is ataxia telengiectasia (Waldman and McIntire, 1972). The genetic defect leading to failure in organ differentiation and maturation in this condition may also give rise to persistent production of AFP by the liver.

Elevated serum AFP levels have also been reported in single patients like amoebic liver abscess, cardiac failure (Adinolfial *et al.*, 1967), idopathic haemochromatosis (Adinolfial *et al.*, 1967). Probably these conditions have affected the liver resulting associated regeneration of liver.

Antenatal diseases

With the use of radioimmunoassay, normal values of AFP in maternal serum and in amniotic fluid have been established. Very high levels of AFP in amniotic fluid and maternal serum (above 800 ng/ml) have been found in intrauterine death, acute and chronic foetal distress and various developmental abnormalities such as anenchephaly, meningomyelocele, hydrocephalus and spinabifida (Seppala and Ruoslahti, 1973).

In spina-bifida, AFP presumably gains access to the amnion via cerebrospinal fluid leakage (Brock and Sutcliffe, 1972) but in other instances, it is probably AFP is being secreted into the amnion via urine (Brock and Sutcliffe, 1972).

High maternal serum concentrations probably originate from the foetus. It is probably due either from increased production by the liver of the distressed foetus or placental leakage or foetal elements or by way of amniotic fluid (Seppala and Ruoslahti, 1973).

It has also been observed that after 13th week of gestation, abortion occurred more frequently in woman with abnormal serum AFP levels (high and low) than in those when AFP concentrations were within normal range (Seppala and Ruoslahti, 1972).

Determination of the circulatory AFP may be used also to differentiate between chorio-carcinoma or hydatidiform mole and normal pregnancy. Although chorionic gonadotrophic hormone is common to all, the serum AFP was found to be elevated only when a foetus was present (Seppala *et al.*, 1972).

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Buffer nerves and spinal cord influences on blood pressure during fluid infusion in dogs

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Sequential changes in blood pressure (BP) were recorded during infusion of normal saline (NS), Ringer Locke (RL) and Tender coconut water (TCW) given at a clinically feasible rate of 0·5 ml/kg/min up to a dose of 100 ml/kg body weight, or more. The fluids were infused to three separate groups each of paraldehyde (PLD) and chloralose-urethane (C and U) anaesthetised dogs. NS infusion had no significant effect on BP under both the anaesthesias, RL increased the BP under both the anaesthesias, while TCW decreased BP in PLD group but had no effect in C and U group. The regression lines fitted to the per cent change in BP had high degree of correlation coefficient (R). The infusions invariably increased the BP during initial stages but the BP decreased towards basal or even below basal level in some cases in later stages of infusion schedule. The TCW infusion was found to be safe in C and U anaesthetised dogs. In vagotomised dogs RL infusion increased BP of PLD group but not in C and U group indicating that vagotomy prevented infusion induced hypertension of C and U group. Carotid sinus (CS) denervation also prevented such RL infusion induced hypertension. The combined vagotomy and CS denervation, however, changed the BP response pattern, in that, the infusion caused initial fall in BP but produced an increase during later stages of infusion. In spinal dogs, the infusion of RL increased BP linearly up to 50 ml stage and then BP decreased with the increasing infusion stage. This BP fall in the later half of infusion schedule could be prevented by simultaneous vagotomy.

Introduction

One of the main aims of fluid infusion is to increase blood pressure (BP) in hypodynamic situations. Warthen (1935); Raisz *et al.* (1950); Guyton *et al.* (1951*a*); Gowdey and Young (1954); Waud (1957) and Guyton (1963) have reported BP increase during various types of fluid infusions. The BP increases rapidly during initial infusion stages; in later stages it becomes either stable or falls to/or below the control BP level (Raisz *et al.*, 1950; Warthen, 1935; Guyton *et al.*, 1951*a*). Some workers (Blalock *et al.*, 1932; Gowdey and Young, 1954) have observed no changes in BP during such infusions. Although the above works have given some knowledge on the effect of infusion on BP, the rate and volume of infusion used during these studies had virtually no relevance to clinical feasibility of such infusions used. Besides, the knowledge on the role of chemical composion of infusion fluid and type of anaesthesia in determining the type of BP response to infusion are lacking. To fill up this lacuna, sequential BP changes during infusion of normal saline (NS), Ringer-Locke (RL) solution and tender coconut water (TCW) (Suresh *et al.*, 1968; Suresh and Hegde, 1971) were studied in intact paraldehyde (PLD) and chloralose and urethane (C and U) anaesthetised dogs. The RL infusion was repeated in vagotomised and/or carotid sinus (CS) denervated and spinal dogs with or without vagotomy to reveal the role of these pathways in the management of the fluid stress.

Material and Methods

Seventy-eight dogs of both sexes and body weights ranging from 7 to 20 kg were divided into 12 groups (G1 to G12) and were used for the study. The BP was recorded continuously either in four channel physiograph with Burdon type pressure transducer (E and M Instrument Co., Houston, Texas) or by mercury monometer on ink writing kymograph. The details of grouping and treatment are given in Table I. PLD was given intramuscularly at 2·2 ml/kg body weight to G1, G2, G3 and G7. The remaining eight groups (Table I) were anaesthetised with C and U after premedication (morphine hydrochloride at 1 mg/kg body weight, subcutaneously) with mixture of C and U prepared in 15 : 85 polyethylene glycol 600 (SD Lab. India), in normal saline. A total of 0·068 to 0·102 g/kg body weight of chloralose (BDH or Kochlight) and 1·02 to 1·52 g/kg urethane (Rediel) was used including the supplementary doses (Suresh, 1978; Suresh and Sharma, 1979*a*) in various dogs.

Intact groups (G1 to G6) : The *basal* preparations in these groups included intra-tracheal intubation, ECG lead attachment *etc.*, as reported by Suresh and Sharma, (1979*a*). The femoral BP recorded in these intact dogs was called the *basal* BP. The experimental surgery groups (G7 to G12) in addition to the basal preparation underwent further surgery as mentioned in Table I (details Suresh and Sharma, 1979*a*). The BP recorded after these surgeries have been called the *new basal* values.

Fluid infusion : Fresh NS, RL (pH 7·4) and TCW were infused at a constant rate (Table I) from a gravity bottle system via femoral vein. TCW was obtained from the tender coconuts fulfilling the requirements prescribed by Suresh *et al.* (1968) and Suresh and Hegde (1971). The TCW was poured out through apical opening and filtered through cotton just before use. Composition of TCW used for infusion was same as reported by Suresh and Sharma (1979*c*).

Analysis of data : The BP changes at each infusion stage were compared with basal and new basal values and the regression curves were fitted to the percentage changes. The statistical methods adopted were same as reported by Suresh (1978).

Results

Table II gives the sequential BP changes during infusion in intact and experimental surgery groups of dogs. Table III gives the basal BP, net percentage changes obtained after experimental surgeries and during infusion schedule, the R values of

Table I. Details of materials and methods

	Intact groups					
	G 1	G 2	G 3	G 4	G 5	G 6
No. of dogs	6	4	4	6	6	6
Anaesthesia	PLD	PLD	PLD	C & U	C & U	C & U
Infusion fluid	NS	RL	TCW	NS	RL	TCW
Rate/ml/kg/min	0·6	0·75	0·6	0·5	0·5	0·5
Maximal dose infused ml/kg	130	140	120	100	100	100

	Experimental surgery groups					
	G 7	G 8	G 9	G 10	G 11	G 12
No. of dogs	9	6	6	6	10	9
Anaesthesia	PLD	C & U	C & U	C & U	C & U	C & U
Experimental surgery performed	I	I	II	I & II	III	III & I
Fluid infused	RL	RL	RL	RL	RL	RL
Rate/ml/kg/min	0·9	0·5	0·5	0·5	0·5	0·5
Maximal dose infused ml/kg	150	100	100	100	100	100

PLD=Paraldehyde; C and U=Chloralose and urethane; NS=Normal saline; RL=Ringer Locke; TCW=Tender coconut water.

I=Vagotomy; II=Carotid sinus denervation, III=C_1 spinal transection.

regression curves and intergroup comparison of net percentage changes. Figs. 1 and 2 give the BP regression curves.

In group G2 and group G4, the infusion caused an initial shift in basal BP and then it remained at that level till the completion and hence there was no regression. Therefore, the net per cent BP change was fitted as regression curve for these two groups. The net per cent BP changes during entire schedule (Tablel III) were markedly different from basal or new basal values, and the groups of dogs under the same anaesthesia had different BP response pattern to NS, RL and TCW infusions. The appreciable BP changes were seen only during RL infusion to intact (G2 and G5), vagotomised (G7), vagotomised-CS denervated (G10) and in spinal dogs (G11 and G12).

Table II. Blood pressure (mm of Hg) at various stages of infusion

G. no.		BV	BV AES	Infusion stages (ml/kg body weight)									
				10	20	30	40	50	60	70	80	90	100
G 1	M/s	112	—	114	109	108	105	103	108	108	107	103	92
		33	—	40	42	31	30	29	42	42	43	29	17
G 2	M/s	132	—	142	153^{a}	154^{b}	155^{a}	146	152^{b}	153^{c}	157^{a}	153^{a}	150^{c}
		22	—	15	19	23	32	32	26	22	27	30	23
G 3	M/s	113	—	128	130	125	125	108	94^{b}	86^{b}	87^{b}	77^{a}	58^{a}
		28	—	49	46	46	48	27	25	14	16	2	13
G 4	M/s	131	—	138	130	132	129	130	140	135	132	132	129
		17	—	19	15	10	9	11	18	12	14	9	11
G 5	M/s	114	—	127^{b}	131^{b}	132^{b}	127^{a}	124^{a}	123	124	119	120	123^{b}
		6	—	12	20	17	18	11	10	9	10	8	6
G 6	M/s	124	—	135	134	122	120	119	123	120	121	120	118
		19	—	21	28	32	27	22	16	15	16	14	17
G 7	M/s	116	113	118	121	124^{e}	129^{bf}	125^{e}	125^{e}	129^{d}	128^{d}	131^{ad}	132^{ad}
		20	23	29	31	27	25	18	20	31	22	19	16
G 8	M/s	114	121	124	120	122	118	117	120	121	120	125	127
		10	11	16	13	16	16	17	15	13	13	15	12
G 9	M/s	112	146^{c}	154^{c}	149^{c}	148^{c}	144^{c}	145^{c}	148^{c}	146^{c}	154^{c}	151^{c}	150^{c}
		11	16	8	8	11	14	13	15	14	14	14	19
G 10	M/s	117	145^{b}	132^{be}	128^{e}	132	148^{a}	152^{c}	160^{c}	160^{c}	145^{b}	147^{c}	154^{b}
		11	22	16	22	29	28	17	14	11	26	12	18
G 11	M/s	127	35^{c}	38^{c}	44^{ca}	61^{cf}	75^{cf}	79^{cf}	75^{ce}	72^{ce}	54^{c}	50^{c}	44^{c}
		21	19	19	19	21	16	16	18	22	20	28	27
G 12	M/s	132	24^{c}	31^{cd}	37^{ce}	49^{cf}	58^{cf}	67^{cf}	73^{cf}	73^{cf}	69^{cf}	64^{cf}	61^{cf}
		16	5	8	11	16	15	17	21	14	16	12	17

M=Group mean; s=Standard deviation. BV=Basal value; BV AES=New basal value after experimental surgery.
^{a}, ^{b}, ^{c}=Significant at 10%, 5%, 1% levels, respectively over the BV.
^{d}, ^{e}, ^{f}=Significant at 10%, 5%, 1% levels, respectively, over the BV AES.
Other abreviations See Table I.

Table III. Blood pressure response to infusion schedule.

	Intact groups						Experimental surgery groups					
	G 1	G 2	G 3	G 4	G 5	G 6	G 7	G 8	G 9	G 10	G 11	G 12
(i)	112	132	113	131	114	124	116	114	112	117	127	132
(ii)	—	—	—	—	—	—	—3·0	6·0	30·0	24·0	—72·4	—81·8
(iii)	—5·3	15·0	—8·7	1·1	9·3	—0·7	8·6	6·7	33·0	25·0	—53·4	—56·5
(iv)	0·73	*	0·97	*	0·65	0·85	0·65	0·92	0·61	0·85	0·94	0·98
G	G 12	G 11	G 3	G 1	G 6	G 4	G 8	G 7	G 5	G 2	G 10	G 9
(v) M	—56·2	—53·4	—8·7	—5·3	—0·7	1·1	6·7	8·6	9·3	15·0	25·0	33·0

(i) Basal BP (mm Hg)

(ii) Per cent change after experimental surgery

(iii) Net per cent change during the entire infusion period.

(iv) R-value of the fitted regression curve, All the R-values are significant at P 0·01

(v) Intergroup comparison of net per cent changes : (Note : (1) Net per cent changes have been arranged in ascending order, (b) values connected by the same line are similar, $P > 0·05$).

G=Group, M=Net per cent change during the entire infusion schedule, *=No regression.

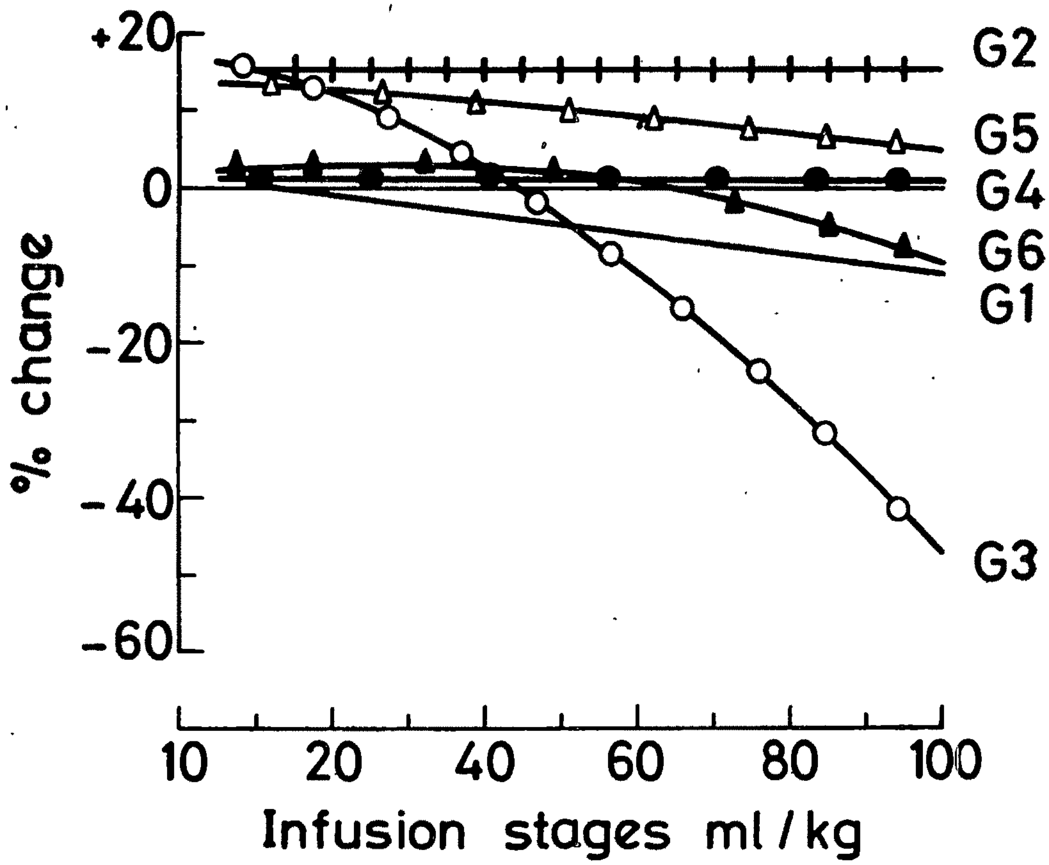

Fig. 1. Regression curves of % changes in basal blood pressure during 0 to 100 ml/kg body weight infusion schedule in intact groups of dogs.

Intact groups—PLD anaesthesia : NS, RL and TCW infusion schedules caused —5·3, 15·0 and —8·7 per cent net changes in basal BP respectively (Table III). The small decrease in basal BP observed during NS infusion (G1, Table II) was not significant, but the consistent increase in BP observed during RL infusion (G2, Table II) were significant at many infusion stages. The BP changes in G2 did not show any regression pattern (Fig. 1). TCW infusion caused a diphasic response of initial increase in BP followed by progressive hypotension till the end of infusion (significant after 55 ml. Table II). Individual variations in response pattern was large. One dog in each group of G1 and G2 did not conform with the group behaviour, and has not been included for analysis.

Intact groups—C and U anaesthesia : Here the saline infusion schedule caused a small net increase in BP (1·0 per cent, not significant, Tables II and III) but did not show any regression pattern (Fig. 1). Similarly, TCW infusion also had no significant (0·7 per

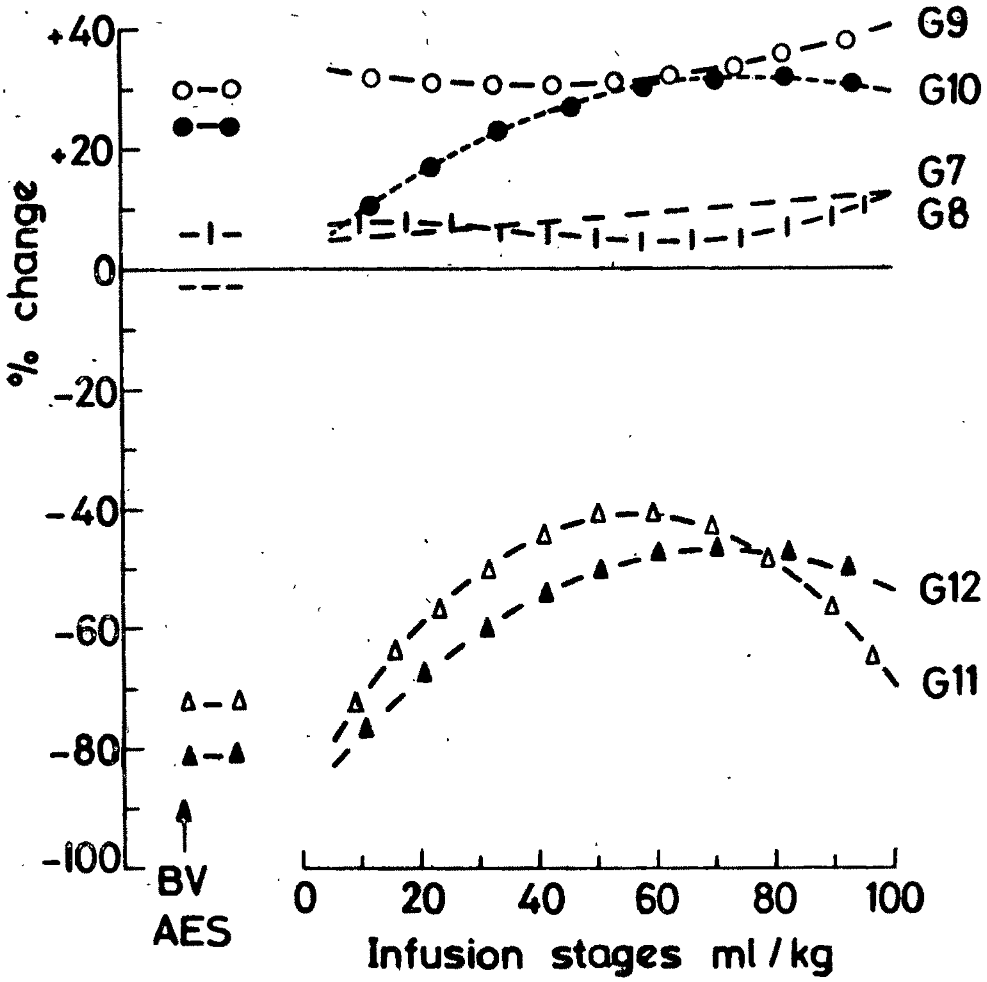

Fig. 2. Regression curves of % changes in blood pressure during 0 to 100 ml/kg body weight of infusion schedule in experimental surgery groups of dogs. AES=Basal value after experimental surgery.

cent net decrease, Table III) effect on BP. Intra-group variations were large in these two groups. However, like in PLD group here also the RL infusion caused sustained significant increase in BP (Table II) giving a 9·3 per cent net increase in BP (Table III).

Experimental surgery groups : The RL infusion significantly increased the new basal BP (8·7 per cent net increase, Table III) of nine vagotomised PLD anaesthetised dogs (G7, Table II). Over 100 ml stage (values not given in Table II), the BP decreased gradually towards basal and fell 2 to 8 per cent below basal level after 125 ml stage till the infusion was stopped at 150 ml/kg stage. In contrast to this, neither the vagotomy *per se* nor the 100 ml infusion schedule had any significant effect on BP in C and U anaesthetised dogs (G8, Table II). The mean BP fell gradually up to 70 ml stage after which it increased gradually (Fig. 2). These vagotomised dogs showed large individual variations.

CS denervation caused a 30 per cent rise in basal BP and this increase continued to be significant throughout the infusion schedule (Table II) and the RL infusion caused only a 3 per cent net increase, over new basal BP (Table III). The BP regression curve resembled that of G8 qualitatively though it occurred at higher new basal BP level. Combined vagotomy and CS denervation (G10) caused a 24 per cent net rise in BP ($P \leqslant 0 \cdot 05$) while the infusion schedule caused only one per cent net increase in new basal BP (Table III). The infusion decreased new basal BP significantly during early stages of infusion schedule but in later stages it increased significantly above it (Table II). This biphasic BP response curve (Fig. 2) was peculiar to this group (G10).

Spinal transection (G11) caused 72·4 per cent fall in basal BP of six dogs included for calculation and the fall continued to be significant throughout the 100 ml/kg infusion schedule (Table II). During infusion schedule the net BP recorded was 53·4 per cent below basal or a 19 per cent net increase in new basal BP (Table III). Infusion caused unsustained 3·3 to 44·3 mm Hg rise over the new basal BP the peak increase being at 45 to 50 ml stages after which it showed a fall. In vagotomised and spinal transected dogs (G12) the effect of surgery and infusion schedule *per se* were qualitatively and quantitatively similar to that seen in spinal dogs (G11, Table II, Fig. 2). However, the peak rise in BP seen during the infusion schedule was higher and more sustained than in G11.

Discussion

Intact groups : The BP response pattern was not uniform in intact groups (Table II and Fig. 1) and appears to depend on the nature of infusion fluid and the anaesthesias. NS infusion to PLD group (G1) decreased the BP progressively but showed almost no effect in C and U group (G4), whereas the RL infusion caused a significant and sustained increase in BP in both PLD and C and U groups (G2 and G5). TCW infusion, which of late has been recommended as plasma volume expander in veterinary practice (Suresh *et al.*, 1968; Suresh and Hegde, 1971; Suresh, 1978), decreased BP in PLD group (G3) but had no significant effect in C and U group (G6). Such differential effects of infusion fluids on BP in dogs under the two anaesthetic regimes have not been reported so far.

The BP regression curves of intact groups (Fig. 1) show that it increased to varying extent during the initial infusion stages and this was invariably followed in later stages by a decrease towards basal or even below basal level, which is similar to response pattern reported by Blalock *et al.* (1932); Warthen (1935); and Raisz *et al.* (1950). However, the actual quantitative comparison of these BP changes could not be made because of basic differences in the type, rate and volume of infusion fluid and anaesthesia used by other workers. Guyton *et al.* (1951*a* and *b*) have suggested that at clinically used rate of fluid infusion, one could not expect a significant rise in BP of normal animals. But the consistent RL infusion induced increase in BP seen in G2 and G5 (Table II) suggests that significant rise in BP could be achieved by slow rate of RL infusion. Absence of significant BP change during NS infusion (G1 and G4) and its significant fall (G3) or no change (G6) during TCW infusion indicates that the infusion effect on BP was probably determined by the composition of infusion fluid. The role of anaesthesia appears to become significant when the electrolyte composition of infusion fluid is not well balanced such as in the case of TCW which contains more K, Ca ions and less sodium ions than blood or plasma (Suresh *et al.*. 1968; and Suresh and Sharma, 1979*c*).

NS infusion caused only minor increase in BP of C and U group (G4) and a linear decrease (not significant) in PLD group (G1). Papper *et al.* (1956) have reported an increase in serum sodium after saline infusion. Sodium ions depress the contractility of heart, favour diastole and causes vasodilatation (Marshall and Shepherd, 1959; and Haddy, 1960); hence failure of BP to rise significantly or a small linear fall seen during saline infusion is probably due to direct depression of heart and blood vessels by Na ions.

The consistent increase in BP during RL infusion might be due to an increase in cardiac output as reported by Gowdey and Young (1954) and Witham *et al.* (1951). The higher net BP increase seen in PLD group (G2) than C and U (G5) could be due to vagolytic activity of PLD or blocking of cholenergic transmission by it as discussed by Suresh and Sharma (1979*a*). In the absence of functional vagal baroreceptor afferents, the inhibition of BP rise by CS afferents may not operate to full extent.

The differential effect of TCW infusion on BP in PLD and C and U groups (G3 and G6) appears to be the anaesthetic effect. During TCW infusion, Suresh and Sharma (1979*c*) have reported large increase in serum Ca^{++}, K^{+} and fall in Na^{+} in PLD group (G3) than in C and U group (G6). High potassium depress the heart and cause vasodilatation (Emanuel *et al.*, 1959; Leonard and Hajdu, 1962). These evidences point out that probably the larger changes in serum electrolytes resulting from TCW infusion to cause such greater hypotension in PLD group (G3) than in C and U group (G6). The present observation that C and U anaesthetised dogs can receive large dose of TCW without deleterious effect and the reports of Suresh *et al.* (1968) and Suresh and Hegde (1971), suggests that fresh TCW could be infused in large doses intravenously. This observation is of practical importance in rural conditions of India where standard fluids for parenteral therapy are not easily available, and even if they are available, the cost is prohibitive for the use by large animal practitioner in such conditions. In these circumstances the TCW could perhaps be used as an easily available and cheap substitute.

Experimental surgery groups : Infusion increased BP significantly in vagotomised dogs under PLD group (G7), vagotomised-CS denervated dogs (G10) and spinal dogs with or without intact vagi (G11 and G12, Table II). The significant increase in BP in G7 appears to be due to improved ventricular filling and cardiac output (Raisz *et al.*, 1950; Witham *et al.*, 1951; Gowdey and Young, 1954). The occurrence of peak BP increase of 14 per cent above basal at 100 ml/kg infusion stage supports this assumption. Incidentally Suresh and Sharma (1979*b*) have reported that these dogs (G7) excreted only 88 ml of urine when compared with 352 and 353 ml produced by G8 and G9 during infusion schedule indicating that more of the infused fluid was retained in G7 dogs. In contrast to increase in BP seen in intact dogs (G5) and vagotomised PLD group (G7) RL infusion had no significant effect in vagotomised (G8) and CS denervated dogs (G9) under C and U anaesthesia. This situation is difficult to account for because the new basal BP of G7 and G8 dogs were similar. One of the possibilities may be the large diuresis reported in them (G8 and G9) by Suresh and Sharma (1979*b*). Adolph and Gerbasi (1933) have reported that urethane increased capillary pressure and dilated the capillaries and veins. This may lead to increased transcapillary fluid loss in these dogs. Guyton *et al.* (1950) and Raisz *et al.* (1950) have reported such rapid loss of infused fluids. The absence of either vagi or CS nerve in these groups appear to make this diuretic and/or diffusion mechanism to operate to a greater extent, because in intact dogs the same RL infusion schedule increases the BP. Hence, in vagotomised (G8) and CS denervated dogs (G9), the RL infusion fails to increase the BP probably because of rapid loss of infused fluid from cardio-vascular system by the way of diuresis and/or transcapillary diffusion.

In vagotomised CS denervated dogs (G10) the infusion caused a biphasic response of initial fall followed by an increase in later stages. Such type of BP regression was not reported earlier. So it appears that in the absence of vagi and CS afferents, the BP changes during infusion are more. Guyton *et al.* (1951*b*) have observed that after pressoreceptor denervation, overloading of cardio-vascular system with fluids decreases the pressure differentials for a given increment of blood volume change. The peripheral blood pressure wave amplitude of vagotomised CS denervated dogs has been reported to decrease further during infusion (Suresh and Sharma, 1980) indicating an increase in sympathetic activity. Based on the available literature (Salzman, 1957; Bartelstone, 1960; Downing and Siegel, 1963; Guyton, 1963; Folkow *et al.*, 1965; and Hainsworth *et al.*, 1973), the following explanation has been suggested to explain this type of regression pattern (*i*) vagotomy and CS denervation *per se* causes maximal systemic vasoconstriction and maximal tachycardia (Suresh, 1975) in the C and U anaesthetised dogs in which urethane has already increased capillary pressure; (*ii*) infusion initally increases the blood volume in the cardiovascular system which is already in maxmal tone. The fluid infusion stress leads to (*a*) thin walled compliance vessels to relaix almost maximally at once resulting in sudden drop in venous return to heart which is already poorly filled because of extreme tachycardia, and/or (*b*) excessive transcapillary fluid loss resulting in sudden decrease in venous return. The BP fall resulting from the above two factors is not fully compensated by increased sympathetic vasomotor tone which is already at high basal tone because of the denervations; (*iii*) as the infusion progresses the increasing fluid volume fills up the capacitance vessels after which a further increase in infusion volume will increase mean systemic pressure (Guyton, 1963) and systemic BP; (*iv*) low diuresis reported for this group (G10) during infusion (Suresh and Sharma, 1979*b*) indicates more fluid retention than in intact dogs (G5), vagotomised dogs (G8) or CS denervated dogs (G9).

The infusion significantly increased the BP of spinal dogs (G11 and G12) though this 100 ml/kg infusion schedule never brought back the BP of spinal dogs to pretransection level at any stage of infusion schedule (Table II and Fig. 2). The BP increased linearly in the first half of the infusion schedule but in later stages it fell towards new basal value. This latter fall was more marked when the vagi were intact (G11). Many workers have reported infusion induced increases in circulatory dynamics and cardiac output in intact dogs (Witham *et al.*, 1951; Fergusen *et al.*, 1953; Gowdey and Young, 1954, Waud, 1957). Gyton *et al.* (1951*b*) have reported a high pressure differential in spinal dogs. Thus, this initial linear increase in BP seen up to 50 to 60 ml/kg body weight infusion dose might be the result of improved cardio-vascular dynamics resulting from infusion to spinal dogs in which there is high pressure differential. Guyton *et al.* (1951*b*) have also reported that the overloading of cardiovascular system with large quantity of fluid to decrease the pressure differentials for given increment of blood volume and this fact may account for less rapid increase in BP during later infusion stages. Though the peak increase in BP observed by Guyton *et al.*, (1951b) compares well with the present observations, a BP plateau of 70 mm Hg below normal in spinal anaesthetised dogs (Guyton *et al.*, 1950) is much higher than the plateau observed in the present study; the differences in techniques employed may account for such difference.

Available evidences (Green *et al.*, 1963; Fine, 1965) indicates that BP fall during the later half of the infusion schedule especially in spinal dogs (G11) resulted from a decrease in cardiac output as a result of widespread capillary damage. Acute T wave changes reported in ECG of G11 dogs (Suresh, 1978) indicate the presence of myocardial hypoxia in these dogs. Opening of collapsed capillary beds when the systemic BP increases beyond critical pressure level and increase in transcapillary permeability due to hypoxic injury might be the other factors involved. Sustained increase in BP seen in vagotomised spinal dogs supports Palmerio *et al.* (1963) observation that vagotomised dogs are more resistant to shock.

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Muscle activity and the H-reflex

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The H-reflex was estimated in 40 rickshaw pullers and in 22 normal controls. The mean value of the index was greater in rickshaw pullers (159·14±3·13) as compared to controls (157·82±3·91). However the difference in the two groups was not statistically significant. It is concluded that muscle hyperactivity does not significantly alter the H-index.

Introduction

Improvement in physical performance as a result or training involves multiple adaptive reactions in the cardiovascular system, the skeletal muscles and the nervous system (Clausen, 1977). Cardiovascular changes like improved myocardial performance, increased cardiac output and reduction in heart rate *etc.* have been well established. So are the changes in skeletal muscle, leading to biochemical adaptations (Holloszy, 1976), hypertrophy and hyperplasia of muscle fibres (Asmussen, 1968).

In the nervous system training produces improvements in motor skills (Morehouse and Miller, 1967). Wedeles (1949) and Edds (1950) demonstrated an increase in the diameter of motor nerve fibres as a result of overloading of the muscles supplied by the nerves. Lastovka (1969) observed increase in the motor nerve conduction velocity in atheletes.

The present study was undertaken to investigate if there is any improvement in reflex activity as a result of training and increased use of muscles. For this purpose the H-reflex was studied in rickshaw pullers (in whom the lower limbs are exposed to heavy exercise) and in controls.

Material and Methods

Reflex activity was studied by electrically induced H-reflex (Smorto and Basmajain, 1972) on 40 rickshaw-pullers. The subjects selected were all young and healthy males. Their age varied from 16 to 25 years. The normal controls were 22 healthy medical students and paramedical staff.

H-latency was recorded by stimulating the posterior tibial nerve percutaneously in the poplitcal fossa, with submaximal stimuli. The stimuli delivered were rectangular pulses varying from 26 to 30 volts in strength and from 0·5 to 1·0 msec in duration. The compound muscle action potential was recorded from the soleus muscle. Disc shaped silver recording electrodes were placed 3 cm apart along the mid-dorsal line of the leg as described by Desmedt (1973). The active electrode was placed proximally. The strength of the stimulus was adjusted so as to obtain both M and H responses simultaneously. Compound muscle action potentials were recorded by a double beam MEDICOR electromyograph with built in stimulator and camera after due amplification. The responses were photographed and enlargements made to facilitate accurate latency measurments. H-latency was measured from the beginning of the stimulus artifact to the start of the evoked H-response. The latency of the M response was measured in a similar manner. As the H-latency and the time interval between H and M responses is influenced by the height of the subject the H-index was calculated using the formula :

$$\text{H index} = \left\{\frac{\text{Height of the subject in cm.}}{\text{Time interval H-M in msec}}\right\}^2 \times 2$$

as described by Guiheneus (1971).

Observations

The values of the H index are shown in the Table. The mean value is greater in rickshaw pullers as compared to controls. However, the difference is not statistically significant. Latency values are almost the same in both groups.

Table. H index and latency values.

Subjects	H index		Latency values in msec			
			H		H-M	
	Mean	S.E.	Mean	S.E.	Mean	S.E.
Rickshaw pullers	159·14	3·13	23·55	0·19	18·97	0·16
Controls	157·82	3·91	23·50	0·30	19·00	0·26

Discussion

Bhatnagar and Anantharaman (1977) in a follow up study of individuals undergoing Yoga training observed an increase in motor conduction velocity with training and quicker relaxation of muscles. Increase in motor conduction velocity with training has been demonstrated in atheletes (Lastovka, 1969). Singh *et al.* (1977) have demonstrated that motor conduction velocity is greater in the dominant limb. According to

Morehouse and Miller (1967) motor skills improve with training not only in the working limb but also in the contralateral limb. These observations suggest the possibility that reflex responses may occur faster after training. However, Kato (1969) who studied the spinal reflex time in atheletes and in controls found no demonstrable differences. The findings of the present study are in agreement with those of Kato (1969).

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Notes and News

Annual Meeting and Convocation

The Annual Meeting and the XVIII Convocation of the National Academy of Medical Sciences (India) were held on March 22 and 23, 1980 at the All India Institute of Medical Sciences, New Delhi. Shri M. Hidayatullah, Vice-President of India was the Chief guest at the convocation.

The Chief Guest distributed Scrolls to the following Fellows and Members and Dr. B.K. Anand, President, admitted them as Fellows/Members respectively :

Fellows

1. Dr. (Mrs.) Vidya N. Acharya
2. Dr. Jasbir Singh Bajaj
3. Dr. (Mrs.) Veena Bijlani
4. Dr. Jadunath Prasad Das
5. Dr. Satya Gupta
6. Dr. Shanti Prakash Gupta
7. Dr. Heeresh Chandra
8. Dr. K. Jagannathan
9. Dr. Chandrakant Ishwerlal Jhala
10. Dr. Brij Mohan Lal Kapur
11. Dr. Surendra Kundan Lal
12. Dr. K. Madhavankutty
13. Dr. Prithipal Singh Maini
14. Maj. Genl. Mohamed Abdul Majid
15. Dr. Radha Charan Mohanti
16. Dr. S.N. Mukherjee
17. Dr. Nabeen Chandra Nayak
18. Surg. Capt. Hardip Singh Nayar
19. Dr. Kul Bhushan Sharma
20. Dr. Harish Chandra Srivastava

Members

1. Dr. Rama Kishan Agrawal
2. Dr. S.K. Aya Ram
3. Dr. A. Balambal
4. Dr. Swapan Kumar Banerjee
5. Dr. Shaik Mohammad Ismail Basha
6. Dr. Yatindra Kumar Batra

7. Dr. G.S. Bhati
8. Dr. S.R. Bhusnurmath
9. Dr. O.P. Chawla
10. Dr. P.K. Chowbey
11. Dr. A.S. Khurana
12. Dr. Ravinder Singh Kohli
13. Dr. Mohan Gopal Rao Koppikar
14. Dr. Krishna Singh
15. Dr. D.K. Mahadik
16. Dr. Krishna Pal Malik
17. Dr. V.G. Mehendale
18. Dr. Usha Kant Misra
19. Dr. Pradip Kumar Mitra
20. Dr. Rajinder Singh
21. Dr. A. Rathnaswami
22. Dr. Y. Nagabhushana Rao
23. Dr. Surinder Mohan Sachdeva
24. Dr. G. Satyanarayan
25. Dr. L.K. Sharma
26. Dr. Rakesh Shukla
27. Dr. C.L. Subbudhi
28. Dr. S.P. Thomas

The following Fellows and Members were admitted as Fellows/Members in absentia :

Fellows

1. Dr. Bangshi Dhar Baruah
2. Dr. P.C. Bhatla
3. Dr. Debi Charan Chowdhury
4. Dr. B.N. Colabawalla
5. Dr. (Mrs.) H. Dhillon
6. Dr. D.R. Doongaji
7. Dr. K. V. Krishna Das
8. Dr. Arcot Gajaraj
9. Dr. R.D. Ganatra
10. Brig. Adhir Kumar Ganguly
11. Dr. M.N. Ghosh
12. Dr. M.G. Gogate
13. Dr. Des Raj Gulati
14. Dr. Ali Mohamad Jan
15. Dr. V. Kalevar

16. Dr. Madhusudan Khadenga
17. Dr. C.R. Krishna Murti
18. Dr. A.N. Mehrotra
19. Dr. G.S. Mutalik
20. Dr. K.G. Nair
21. Dr. K.N. Pai
22. Dr. N.S. Pathania
23. Dr. S.R. Rege
24. Dr. G.C. Sepaha
25. Dr. Syed Naseer Ahmed Shah
26. Dr. V.N. Sharma
27. Dr. A.K.N. Sinha
28. Dr. K.S. Subramaniam
29. Dr. N. Zaman

Members

1. Dr. Ravindra Ramakrishna Abhyankar
2. Dr. N. Ananthakrishna
3. Dr. T.S. Aughusthy
4. Major K.S. Bhagiana
5. Dr. S.M. Bhat
6. Dr. C.V. Bhiramanandham
7. Dr. J.B. Daniel
8. Dr. Ashok Kumar Das
9. Dr. Rajiv Dhand
10. Dr. M. Dhanraj
11. Dr. T. Dhinakaran
12. Dr. N. Durai Raj
13. Dr. V. Dwarakanath
14. Dr. N. Elangevan
15. Dr. R.R. Evangeline
16. Dr. S.M.A. Gilani
17. Dr. M.S. Hiremath
18. Dr. B. Indiradevi
19. Dr. Alexander T. John
20. Dr. A.V. Kamath
21. Dr. Uma Devi Karunakaran
22. Dr. C.B. Khare
23. Dr. Philip Korula
24. Dr. K.V. Krishna Raj
25. Dr. B. Krishna Raj
26. Dr. V.D. Krishnaram
27. Dr. V. Kumaraswami

28. Dr. D.K.S. Kusurkar
29. Dr. P.D. Lakdawala
30. Dr. A. Mahakrishnan
31. Dr. R. Muthulakshmi
32. Dr. P. Nadarajan
33. Dr. T.N. Prabhakaran Nair
34. Dr. Sambasiva Padma
35. Dr. A.P. Pandya
36. Dr. Ajit Kumar Ramagounda Patil
37. Dr. A. Marthanda Pillai
38. Dr. S. Manakavala Parumal Pillai
39. Dr. G. Mathi Prakasam
40. Dr. N.R. Potty
41. Dr. N. Radhakrishnan
42. Dr. A.S. Rajagopal
43. Dr. Sarala Rajajee
44. Dr. M. Ramachandran
45. Dr. S. Ram Kumar
46. Dr. J.N. Rao
47. Dr. Maheswari Ravi
48. Dr. (Mrs.) Shanti Roy
49. Dr. Manabendra Roy
50. Dr. Vinay Sakhuja
51. Dr. G. Sarangi
52. Dr. C.K. Sasidharan
53. Dr. Vatsala Niranjan Shah
54. Dr. R.S. Sharma
55. Lt. Col. Sampuran Singh
56. Dr. Ram Gopal Singh
57. Dr. V. Sivaparakash
58. Dr. K.C. Sood
59. Dr. P.S. Sreemathi
60. Dr. G.V. Sridharan
61. Dr. S. Subbiah
62. Dr. Robin B. Talati
63. Lt. Col. Ved Prakash Taneja
64. Surg. Ldr. S.J. Thomas
65. Dr. Thomas Titus
66. Dr. P.H. Trivedi
67. Dr. R.P. Usgaocar
68. Lt. Col. Harbans Singh Uberoi
69. Dr. P. Viswanathan
70. Dr. Pramod Madhav Velenkar
71. Dr. P.A. Vinod Kumar

The Vice-President M. Hidayatullah also distributed the following awards for the year 1979-80 :

(*a*) The Academy Oration Award to Dr. R. Subramaniam, M.D., F.R.C.P., F.A.M.S., Hon. Physician to the President of India, 8-C Balfour Road, Madras. Dr. Subramaniam delivered his oration on "Some aspects of nutritional cirrhosis of liver" on March 22, 1980.

(*b*) The Glaxo Oration Award to Dr. B.K. Aikat, M.D., D.C.P., Ph.D., F.A.M.S., Retd. Director-Professor of Pathology, Postgraduate Institute of Medical Education and Research, Chandigarh. Dr. Aikat delivered his oration "Kala Azar in Bihar", on March 23, 1980.

(*c*) The Shriram Memorial Oration Award to Dr. O.P. Gupta, M.D., F.R.C.P., F.I.C.A. F.C.C.P., F.A.M.S., Director of Medical Education and Research (Govt. of Gujarat), Ahmedabad. Dr. Gupta delivered his oration on "Diabetes and Nutrition," on March 23, 1980.

(*d*) The Prof. R.V. Rajam's 80th Birthday Memorial Oration Award to Dr. D. Jaganatha Reddy, M.D., F.R.C. Path., F.A.M.S., Director and Pathologist, Vijay Hospital, Madras. Dr. Reddy delivered his oration on "Whither Health Care for the Millions", on March 23, 1980.

(*e*) The Achanta Lakshmipathi Oration Award to Dr. Sarada Subrahmanyam, M.D., F.R.C.P. (Lond.), F.A.M.S., Professor and Head of the Department of Physiology, Postgraduate Institute of Basic Medical Sciences, Taramani, Madras. Dr. Subrahmanyam delivered her oration on "Neurohumoral Correlates of Behaviour", on March 23, 1980.

(*f*) The Dr. S.S. Misra Memorial Medal and cash prize to Dr. Dipika Mohanty, Asstt. Professor of Haematology, Postgraduate Institute of Medical Education and Research, Chandigarh, for her unpublished paper entitled "Effect of experimentally induced folate deficiency on the female reproductive organs. Cytomorphological, cytokinetic and hormonal studies". Dr. Mohanty presented her paper on March 23, 1980.

(*g*) The Shriram Memorial Medal and cash prize was awarded in absentia to Dr. Raj Narain, FAMS, Retd. Project Director, Tuberculosis Prevention Trial, Bangalore for his published paper entitled "Mortality due to Tuberculosis in Indian Children", *Tubercle*, London, **85**, 1977, pp 187-189.

Continuing Education

A Session on Continuing Education was held under the Chairmanship of Dr. B.K. Anand, FAMS, on March 22, 1980. Dr. V.T.H. Gunaratne, Regional Director, World Health Organization, New Delhi, inaugurated the session. Dr. Gunaratne informed that the W.H.O. would consider giving a grant of $ 10,000 to the Academy for organizing courses at various Chapters of the Academy.

Indian Society of Hematology and Blood Transfusion

Joint Annual Hematology Congress will be held at Birla Krida Kendra, Bombay on 5, 6, 7 December, 1980. During the conference Symposia on "Nutritional Anemia" and "Acquired Coagulation Disorders" are planned. Last dates for sending abstracts of papers and registration are 30.9.1980 and 15.11.1980 respectively. Prior to conference on 3, 4, December, 1980 a Workshop on "Laboratory Investigations of Hemoglobinopathies" will be organised. For details write to : Dr. B.C. Mehta, Jt. Org. Secretary, Hematology Department, K.E.M. Hospital, Bombay-400 012.

Achievements of Fellows and Members of the Academy

Dr. S.P. Pamra, FAMS, has been appointed Editor of the Indian Journal of Tuberculosis. He has also been nominated Corresponding Member of the Scientific Committee on Treatment of the International Union against Tuberculosis, Paris.

Col. Kirpal Singh, FAMS, has been elected as a Fellow of the Royal Australian and New Zealand College of Psychiatrists. In September 1979, he was invited by the North Western University, Chicage and University of Pensylvania, Philadelphia, to give lectures at their medical schools. These lectures were well received.

Dr. P. Upadhyaya, FAMS, has been elected Member of the Governing Body of the Association of Surgeons of India. He was invited to chair a Symposium at the 5th Asian Congress of Paediatric Surgery held at Karachi, Feb. 17-19, 1980. Dr. Upadhyaya was also invited to speak in the plenary session on Interaction between developed and developing countries and chair the Symposium on hydrocephalus at World Congress of Paediatric Surgery. He has also been elected Secretary General, Asian Association of Paediatric Surgeons at Karachi.

Dr. B.M.S. Bedi, MAMS, has been awarded the Glaxo Oration award by the Indian Association of Dermatologists, Venereologists and Leprologists for outstanding scientific contribution.

Dr. B.N.S. Walia, MAMS, has been appointed Corresponding Editor, Journal of Tropical Pediatrics and Child Health, London. He has also been appointed Member of the Editorial Board of the Indian Journal of Pediatrics. Dr. Walia was invited to attend International Seminar on Delivery of Health Care at Islamabad, Pakistan. He also represented the Indian Academy of Pediatrics at the meeting of the Association of Pediatric Societies of South East Asia Region, Bangkok. He was also invited to attend 3rd Asian Congress of Pediatrics, Bangkok.

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NATIONAL ACADEMY OF MEDICAL SCIENCES (INDIA)

C-II/16, Ansari Nagar, Medical Enclave, New Delhi-110029.

IMPORTANT NOTICE

N.A.M.S. AWARDS 1980-81

The Academy will be awarding the following during the current year :-

1. **Dr. S.S. Misra Memorial Award :** This award has been established to perpetuate the memory of late Dr. S.S. Misra, a Founder Fellow of the Academy; the award is in the form of a bronze medal and cash prize for the best unpublished work in any field of Bio-Medical Research by a bio-medical scientist below 40 years. Those enteries which do not qualify for the Award may be awarded merit certificates.
2. **Sir Shriram Memorial Award :** This award has been established by the Shriram Foundation and the Academy will award a bronze medal and cash prize to a bio-medical scientist for the best published work on Community Medicine (Community Health), Medical Education and Hospital Administration done in India, during the preceding three years. In case of joint papers, scrutiny will only be done if the candidate is the first author. There is no age restriction.
3. **Dr. R.M. Kasliwal Award :** The award has been funded by Dr. R.M. Kasliwal, founder Fellow, and is awarded to the best worker in the area of : *Colon and its Diseases.* The candidate will be required to submit with the paper, a complete bibliography on the subject including work done in India. There is no age restriction.
4. **Dr. Vimla Virmani Award :** The award has been funded by Dr. Vimla Virmani, a Fellow, and is in the form of a bronze medal and cash prize to be awarded to a Bio-Medical Scientist below the age of 45 years for outstanding work in the field of : *Rehabilitation of Neurologically Handicapped Patients,* based on published or unpublished work with particular emphasis on the applicability of the work, under socio-cultural and economic conditions prevalent, to the Indian community.

Conditions

I. The Scientist should not have received any prize for the same paper(s) in the past;

II. Four copies of each paper should reach the Office of the Academy latest by the 30th September, 1980, accompanied by a forwarding letter giving a brief bio-data of the Scientist alongwith the title of Medal/Prize for which the paper is submitted;

III. Selected papers for Dr. S.S. Misra Memorial Bronze Medal/Certificate of Merit and unpublished papers for Dr. Vimla Virmani Award will be published in the 'ANNALS' of the National Academy of Medical Sciences;

IV. Scientists selected for medal/prize or Certificates of Merit will be invited by the Academy to present the papers at the Annual meeting of the Academy in March, 1981 and the Academy will meet cost of travel.

V. The award will be formally presented at the time of the Convocation of the Academy.

Academy Publications

Liver Cirrhosis—Proceedings of the Symposium held on 5-6 February, 1966 Agra, India, Ed. P.N. Wahi. Pages : 190. Price : Rs. 8.00

Tuberculosis of the Nervous System—Monograph on the Proceedings of the Symposium held on 2-5 February, 1972 at Bombay, India. Eds. C.C. Kapila, D.K. Dastur, Baldev Singh and P.N. Tandon. Pages : 310. Price : 20.00 or $ 5.00

Non-Cirrhotic Portal Fibrosis with Portal Hypertension—Eds. A.K. Basu and B.N. Guharary. Pages : 319. Price. Rs. 30.00 (Paper back); Rs. 40.00 (Cloth bound)

NATIONAL ACADEMY OF MEDICAL SCIENCES (India)
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INSTRUCTIONS TO AUTHORS OF REVIEW PAPERS

The review papers to be published in Annals of the NAMS, are usually invited by the Editor after considering the recommendations of the Working Editorial Group. Experts on all aspects in bio-medical sciences are considered for this purpose. Others who have interests in writing review papers dealing mainly with the current status of his/her subject of interest are also encouraged to send such articles. The latter manuscripts are reviewed by two or more experts in the field and ultimate decision about publication is guided by their recommendations.

For the invited authors to write a review article a deadline of one month is usually given, and the authors are requested to follow the deadline. If necessary, the author should write to the Editor immediately for setting a new deadline. The usual lengt of printed pages should range maximum between 10 and 15 pages. Two copies of the manuscript should be submitted to : The Chief Editor, Annals of the National Academy of Medical Sciences (India), C-II/16, Ansari Nagar, New Delhi-110029.

A. **Manuscripts** should be type written carefully in double spacing on one side of the paper of uniform size and with sufficient margin.

(a) **Title page** should be separate, giving title of the paper, names of the authors, Laboratory/Institutes of origin with city and complete address. The running title should also be given on this page.

(b) **Introduction** must precede the text highlighting the scope and significance of the paper and the essential background necessitating writing of the review.

(c) **The text of the review** should be sufficiently precise, selective and all references relevant to the subject uptodate should be mentioned. The article should be a critical review, mentioning conflicting points of view if any, change of accepted concepts, and the current status of the subject under review. Illustrations, diagrams and tables may be used to elaborate the present concept.

(d) **Summary** should also highlight the lacunae in the knowledge and avenues for further work in that particular area.

(e) **References** as per the style of the Journal. (*see* Instructions to Authors).
B, C and D : *see* Instructions to Authors.

INSTRUCTIONS TO AUTHORS

The Annals of the National Academy of Medical Sciences (India), appearing quarterly welcomes well-organized original contributions on all topics in biomedical sciences. Manuscript should be typewritten carefully in double spacing on one side of the paper of uniform size and with sufficient margin. Two copies of the manuscript complete with figures and tables should be submitted to : The Editor, Annals of the National Academy of Medical Sciences (India), C-II/16, Ansari Nagar, New Delhi 110029. Submission of a manuscript in this journal implies that it has not been published and is not under consideration for publication elsewhere.

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A. **Manuscripts :** Title page should be separate, giving title of the paper, names of the authors, laboratory/Institute of origin with city and complete address. The running title should also be given on this page. Every article must be preceded by an abstract not exceeding 200 words. It should indicate the scope and significant content of the paper, highlighting the principle findings and conclusion. Text should in general, contain an Abstract, Introduction, Material and Methods, Results, Discussion, Acknowledgment if any, and References.

Introduction should be brief and state precisely the scope of the paper and the essential background necessitating investigation done.

Material and Methods should be described briefly and reference to the sources (*e.g.* Sanyal, 1970) should be given. New matters however, may be given in detail.

Results should be brief and only relevant data should be given. The data should be statistically analysed, and the P value should be given.

Tables should be short and restricted in number. An illustration (photographs or line drawing) should be about 1½ time the reproducible size. Glossy prints of photographs are preferred. Any lettering or annotation on photographs or line drawings should be indicated on a tracing paper or a legend sheet. The name of the principle author and the figure number should be written on the back of the illustrations.

Discussion should be logical and should be related to the significance to the work done.

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Chakravarty, N., Goth, A. and Sen, P. 1973. Potentiation of dextran induced histamine release from rat mast cells by phosphatidyl serine. *Acta Physiol Scand* **88**, 496.

Sen, P. and Sanyal, R.K. 1969. Experimental studies on antigenicity of penicillin, *In Aspects of Allergy and Applied Immunology* **2** 123. Edited R. Viswanathan, R.K. Sanyal, G. Bazaz-Malik, S. Arora and P.D. Miglani, New Heights, Delhi.

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